```
=> s asthma or bronchial disease or bronchodilator?
L11      101536 FILE MEDLINE
L12       76683 FILE BIOSIS
L13       88372 FILE EMBASE
L14       34724 FILE CAPLUS

TOTAL FOR ALL FILES
L15      301315 ASTHMA OR BRONCHIAL DISEASE OR BRONCHODILATOR?

=> s eotaxin 1 or eosinophil(l)chemotactic(l)(factor or protein) or gene scya11
protein
L16        1119 FILE MEDLINE
L17         770 FILE BIOSIS
L18         860 FILE EMBASE
L19         761 FILE CAPLUS

TOTAL FOR ALL FILES
L20        3510 EOTAXIN 1 OR EOSINOPHIL(L) CHEMOTACTIC(L)(FACTOR OR PROTEIN) OR
                GENE SCYA11 PROTEIN

=> s erk 1 or erk1 or cek1 protein (l)candida albican? or fungal protein or mitogen
activat? protein kinase 3
L21       33257 FILE MEDLINE
L22        8393 FILE BIOSIS
L23       10344 FILE EMBASE
L24       11476 FILE CAPLUS

TOTAL FOR ALL FILES
L25       63470 ERK 1 OR ERK1 OR CEK1 PROTEIN (L) CANDIDA ALBICAN? OR FUNGAL
                PROTEIN OR MITOGEN ACTIVAT? PROTEIN KINASE 3

=> s (eosinophil or granulocyte?)(l)(recruit? or function?)
L26       12376 FILE MEDLINE
L27       11541 FILE BIOSIS
L28       11544 FILE EMBASE
L29        9145 FILE CAPLUS

TOTAL FOR ALL FILES
L30       44606 (EOSINOPHIL OR GRANULOCYTE?)(L)(RECRUIT? OR FUNCTION?)

=> s l5 and l10
L31           4 FILE MEDLINE
L32           3 FILE BIOSIS
L33           4 FILE EMBASE
L34           4 FILE CAPLUS

TOTAL FOR ALL FILES
L35          15 L5 AND L10


=> dup rem l35
PROCESSING COMPLETED FOR L35
L36           4 DUP REM L35 (11 DUPLICATES REMOVED)

=> d ibib abs 1-4;s l5 and l15

L36  ANSWER 1 OF 4     MEDLINE on STN                    DUPLICATE 1
ACCESSION NUMBER:    2004185966     MEDLINE Full-text
DOCUMENT NUMBER:     PubMed ID: 15081532
TITLE:               Down-modulation of the antigen receptor by a superantigen
```

for human B cells.
AUTHOR: Viau Muriel; Cholley Beatrice; Bjorck Lars; Zouali Moncef
CORPORATE SOURCE: Institut National de Sante et de Recherche Medicale, Immunopathologie Humaine, 15 rue de l'Ecole de Medecine, 75006 Paris, France.
SOURCE: Immunology letters, (2004 Mar 29) 92 (1-2) 91-6.
Journal code: 7910006. ISSN: 0165-2478.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200411
ENTRY DATE: Entered STN: 20040415
Last Updated on STN: 20041219
Entered Medline: 20041124

AB B cell superantigens (SAgs) have been implicated in human diseases by demonstrating non-clonotypic expansion of B cells bearing certain immunoglobulin variable region genes. One possibility is that, during infection with microorganisms secreting SAgs, these potent molecules might modulate BcR expression. To test this hypothesis, we investigated the potential effects of a SAg, protein L from Peptostreptococcus magnus, on antigen B cell receptor (BcR) surface expression in vitro. Using fluorescence microscopy, we found that this SAg induced down-regulation of BcR expression. This effect was time-, dose-, and temperature-dependent, and shedding of cell surface IgM molecules into the culture supernatant was not detected. These data demonstrate that SAg-mediated down-regulation of the BcR expression occurs primarily as a result of BcR internalization. In addition, two specific inhibitors of protein tyrosine kinases were found to retard the BcR modulation on the cell surface and inhibit SAg-induced receptor internalization, showing that tyrosine phosphorylation is required for subsequent internalization of mIg-ligand complexes. The down-modulation of BcR expression may have pathological consequences in patients infected with microorganisms secreting SAgs.

L36 ANSWER 2 OF 4 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 2001690659 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 11739530
TITLE: CXCR3 internalization following T cell-endothelial cell contact: preferential role of IFN-inducible T cell alpha chemoattractant (CXCL11).
AUTHOR: Sauty A; Colvin R A; Wagner L; Rochat S; Spertini F; Luster A D
CORPORATE SOURCE: Division of Rheumatology, Allergy, and Immunology, Center for Immunology and Inflammatory Diseases, Massachusetts General Hospital, Harvard Medical School, Charlestown, MA 02129, USA.
CONTRACT NUMBER: CA69212 (NCI)
DK50305 (NIDDK)
SOURCE: Journal of immunology (Baltimore, Md. : 1950), (2001 Dec 15) 167 (12) 7084-93.
Journal code: 2985117R. ISSN: 0022-1767.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200112
ENTRY DATE: Entered STN: 20011213
Last Updated on STN: 20020123
Entered Medline: 20011227

AB Chemokine receptors are rapidly desensitized and internalized following ligand binding, a process that attenuates receptor-mediated responses. However, the physiological settings in which this process occurs are not clear. Therefore, we examined the fate of CXCR3, a chemokine receptor preferentially expressed on activated T cells following contact with endothelial cells. By immunofluorescence microscopy and flow cytometry, we found that CXCR3 was rapidly internalized when T cells were incubated with IFN-gamma-activated human saphenous vein endothelial cells (HSVEC), but not with resting HSVEC. Similar results were obtained using human CXCR3-transfected murine 300-19 B cells. CXCR3 down-regulation was significantly more pronounced when T cells were in contact with HSVEC than with their supernatants, suggesting that CXCR3 ligands were efficiently displayed on the surface of HSVEC. Using neutralizing mAbs to IFN-induced protein-10 (CXCL10), monokine induced by IFN-gamma (CXCL9), and IFN-inducible T cell alpha chemoattractant (I-TAC; CXCL11), we found that even though I-TAC was secreted from IFN-gamma-activated HSVEC to lower levels than IFN-induced protein-10 or the monokine induced by IFN-gamma, it was the principal chemokine responsible for CXCR3 internalization. This correlated with studies using recombinant chemokines, which revealed that I-TAC was the most potent inducer of CXCR3 down-regulation and of transendothelial migration. Known inhibitors of chemokine-induced chemotaxis, such as pertussis toxin or wortmannin, did not reduce ligand-induced internalization, suggesting that a distinct signal transduction pathway mediates internalization. Our data demonstrate that I-TAC is the physiological inducer of CXCR3 internalization and suggest that chemokine receptor internalization occurs in physiological settings, such as leukocyte contact with an activated endothelium.

L36 ANSWER 3 OF 4 MEDLINE on STN DUPLICATE 3
ACCESSION NUMBER: 2002111753 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 11843178
TITLE: Mig-6 is a negative regulator of the epidermal growth factor receptor signal.
AUTHOR: Hackel P O; Gishizky M; Ullrich A
CORPORATE SOURCE: Department of Molecular Biology, Max-Planck-Institute of Biochemistry, Martinsried, Germany.
SOURCE: Biological chemistry, (2001 Dec) 382 (12) 1649-62. Journal code: 9700112. ISSN: 1431-6730.
PUB. COUNTRY: Germany: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200207
ENTRY DATE: Entered STN: 20020215
Last Updated on STN: 20020717
Entered Medline: 20020716

AB In contrast to signal generation and transmission, the mechanisms and molecules that negatively regulate receptor tyrosine kinase (RTK) signaling are poorly understood. Here we characterize Mig-6 as a novel negative feedback regulator of the epidermal growth factor receptor (EGFR) and potential tumor suppressor. Mig-6 was identified in a yeast two-hybrid screen with the kinase active domain of the EGFR as bait. Upon EGF stimulation Mig-6 binds to the EGFR involving a highly acidic region between amino acids 985-995. This interaction is kinase activity-dependent, but independent of tyrosine 992. Mig-6 overexpression results in reduced activation of the mitogenactivated protein kinase ERK2 in response to EGF, but not FGF or PDGF, stimulation and in enhanced receptor internalization without affecting the rate of degradation. The induction of Mig-6 mRNA expression in response to

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L43          30 FILE BIOSIS
L44          44 FILE EMBASE
L45          65 FILE CAPLUS

TOTAL FOR ALL FILES
L46         168 L5 AND ASTHMA

=> s l41 or l46
L47          29 FILE MEDLINE
L48          30 FILE BIOSIS
L49          44 FILE EMBASE
L50          67 FILE CAPLUS

TOTAL FOR ALL FILES
L51         170 L41 OR L46

=> s l51 range=(,2003)
'(,2003)' IS NOT A VALID RANGE FOR FILE 'MEDLINE'
Valid RANGE values are file specific.  For more information, enter
HELP RANGE or HELP SET RANGE at an arrow prompt (=>) in the current
file.
ENTER RANGE FOR FILE 'MEDLINE' OR (ALL):end
SEARCH ENDED BY USER
L52          18 FILE BIOSIS
L53          20 FILE EMBASE
L54          36 FILE CAPLUS

TOTAL FOR ALL FILES
L55          74 L51


=> dup rem l55
PROCESSING COMPLETED FOR L55
L56           48 DUP REM L55 (26 DUPLICATES REMOVED)

=> d 1-48 ibib abs;s l20 and l25

L56  ANSWER 1 OF 48  CAPLUS  COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER:         2003:875074  CAPLUS Full-text
DOCUMENT NUMBER:          139:380024
TITLE:                    Oligonucleotide probes and primers for diagnosing and
                          monitoring autoimmune and chronic inflammatory
                          diseases
INVENTOR(S):              Wohlgemuth, Jay; Fry, Kirk; Woodward, Robert; Ly, Ngoc
PATENT ASSIGNEE(S):       Expression Diagnostics, Inc., USA
SOURCE:                   PCT Int. Appl., 877 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   9
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.         DATE
     ---------------      ----   --------    --------------------    --------
     WO 2003090694         A2    20031106    WO 2003-US13015         20030424
     WO 2003090694         A3    20041118
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM,
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PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2004009479	A1	20040115	US 2002-131827	20020424
US 6905827	B2	20050614		
JP 2005523038	T2	20050804	JP 2003-587333	20030424
PRIORITY APPLN. INFO.:			US 2002-131827	A2 20020424
			US 2001-296764P	P 20010608
			US 2001-6290	A2 20011022
			WO 2003-US13015	W 20030424

AB Methods of diagnosing or monitoring auto immune and chronic inflammatory diseases, particularly systemic lupus erythematosus and rheumatoid arthritis, in a patient by detecting the expression level of one or more genes in a patient, are described. Oligonucleotide probes and primers for diagnosing or monitoring autoimmune and chronic inflammatory diseases, particularly systemic lupus erythematosus and rheumatoid arthritis and kits or systems containing the same are also described. In one format, the gene expression system is immobilized on an array, e.g. a chip, plate, bead, pin, membrane, microfilter, oligonucleotide, cDNA, or polynucleotide microarray.

L56 ANSWER 2 OF 48 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:696523 CAPLUS Full-text
DOCUMENT NUMBER: 139:229271
TITLE: Signature genes expressed the lung during asthma or allergies and their use in predicting, diagnosing and treating asthma or allergies
INVENTOR(S): Rothenberg, Marc Elliot; Zimmermann, Nives
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 36 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20031665662	A1	20030904	US 2003-377998	20030228
CA 2477400	AA	20030912	CA 2003-2477400	20030228
WO 2003073990	A2	20030912	WO 2003-US6183	20030228
WO 2003073990	A3	20050310		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

EP 1527196	A2	20050504	EP 2003-711317	20030228
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
JP 2005532997	T2	20051104	JP 2003-572512	20030228

PRIORITY APPLN. INFO.: US 2002-361606P P 20020301
WO 2003-US6183 W 20030228

AB Several genes are upregulated in the lung of asthma or allergy sufferers. Many of the genes up-regulated in asthma are involved in arginine metabolism in the lung. Moreover, a set of 291 signature genes was found that can be used to indicate a patient's predilection for developing asthma or the patient's degree of suffering. Also, a set of 59 signature genes were found that indicate a patient's predilection for developing allergies. Many of the up-regulated genes relating to asthma were from the arginine metabolic pathway. Other genes, such as ADAM8, SPRR2A and SPRR2B were also strongly up-regulated in asthma. Treatment of asthma may be accomplished by administering compns. which decrease the levels of Arginase I, Arginase II, cationic amino acid transporter CAT2, or other arginase pathway members in the lung. Addnl., detection of altered levels of these proteins or the mRNA encoding them may be useful to diagnose the presence of asthma in a patient.

L56 ANSWER 3 OF 48 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:511974 CAPLUS Full-text
DOCUMENT NUMBER: 139:64466
TITLE: Global expression analysis of extracellular matrix-integrin interactions in monocytes
INVENTOR(S): Defougerolles, Antonin; Gotwals, Philip; Green, Cynthia; Koteliansky, Victor
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 22 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003124726	A1	20030703	US 2001-924168	20010803
PRIORITY APPLN. INFO.:			US 2000-222874P P	20000803

AB The invention is based in part on the discovery that certain nucleic acids are differentially expressed in monocyte cell line THP-1 when exposed to various extracellular matrix components (fibronectin, type I collagen, laminin, and VCAM) in the presence or absence of growth factors. Following culture of THP-1 cells in the presence of integrin modulating agent, cDNA was prepared and the resulting samples were processed using GeneCalling® differential expression anal., which couples expression profiling with a database query which utilizes fragment length and end sequence information to provide immediate feedback on expressed genes. Global gene expression anal. enabled quantification of the relative contribution of integrin-mediated cell attachment to changes in gene expression. The pos. identification of over 140 genes and ESTs whose expression in monocytes is induced by attachment to extracellular matrix not only represents a significant increase in the number of genes previously identified, but also reveals the importance of ECM-integrin interaction in multiple aspects of monocyte biol. Thus, the invention provides methods of identifying integrin modulating agents using differential gene expression. Also disclosed are method of treating atherosclerosis and inflammatory disorders in a subject.

L56 ANSWER 4 OF 48 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:241991 CAPLUS Full-text
DOCUMENT NUMBER: 138:270283
TITLE: Oligodeoxynucleotide and its use to induce an immune

response

INVENTOR(S): Klinman, Dennis; Verthelyi, Daniela; Ishii, Ken; Mond, James J.; Gursel, Mayda

PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 52 pp., Cont.-in-part of U.S. Ser. No. 958,713.
CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 2003060440	A1	20030327	US 2002-68160		20020206
US 2005209184	A1	20050922	US 2005-131672		20050517
PRIORITY APPLN. INFO.:			US 1999-128898P	P	19990412
			US 2001-958713	A2	20011011
			WO 2000-US9839	W	20000412
			US 2002-68160	A1	20020206

AB D type CpG oligodeoxynucleotides are provided herein that include a sequence represented by the following formula: 5'- X1X2X3Pu1Py2CpGPu3Py4X4X5X6(W)M(G)N-3' wherein the central CpG motif is unmethylated, Pu is a purine nucleotide, Py is a pyrimidine nucleotide, X and W are any nucleotide, M is any integer from 0 to 10, and N is any integer from 4 to 10. The oligodeoxynucleotides can activate immune cells, such as antigen-presenting cells or natural killer cell, and/or can stimulate production of cytokines. Methods of using these oligodeoxynucleotides to induce an immune response are provided. The oligodeoxynucleotides can be used in treatment or amelioration of cancer, allergy, autoimmune disease, immunodeficiency, or infection. They can also be used to enhance the efficacy of vaccines.

L56 ANSWER 5 OF 48 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
DUPLICATE 1

ACCESSION NUMBER: 2003:549893 BIOSIS Full-text

DOCUMENT NUMBER: PREV200300538371

TITLE: Interleukin-12-independent down-modulation of cockroach antigen-induced asthma in mice by intranasal exposure to bacterial lipopolysaccharide.

AUTHOR(S): Lundy, Steven K.; Berlin, Aaron A.; Lukacs, Nicholas W. [Reprint Author]

CORPORATE SOURCE: Department of Pathology, University of Michigan Medical School, 1301 Catherine St., 5214 Medical Sciences I, Ann Arbor, MI, 48109, USA
nwlukacs@umich.edu

SOURCE: American Journal of Pathology, (November 2003) Vol. 163, No. 5, pp. 1961-1968. print.
ISSN: 0002-9440 (ISSN print).

DOCUMENT TYPE: Article

LANGUAGE: English

ENTRY DATE: Entered STN: 19 Nov 2003
Last Updated on STN: 19 Nov 2003

AB Several studies have shown that exposure to bacterial lipopolysaccharide (LPS) can either prevent or inhibit asthma in humans and laboratory rodents. Much emphasis has been placed on the role of cytokines and chemokines in the establishment and maintenance of allergic airway disease. Therefore, it is of interest to study the role of LPS in affecting airway pathology and lung cytokine and chemokine responses in the maintenance phase of asthma. Increasing doses of LPS were administered into the airways of mice

presensitized with cockroach allergen (CRAg), then allergic airway disease parameters were assessed after CRAg challenge. Airway hyperresponsiveness after antigen challenge decreased at the highest dose of LPS tested, which was accompanied by a decrease in airway and lung eosinophils. However, a dramatic increase in lung inflammation because of neutrophil influx was observed. Measurement of cytokines in lungs of LPS-treated, CRAg-sensitized mice indicated that interleukin (IL)-12 levels were increased by LPS treatment in a dose-dependent manner, as were levels of several inflammatory chemokines. In contrast, levels of IL-4, 11-13, 11-5, and IL-10 were reduced in whole lung homogenates only of high-dose LPS-treated mice. Intranasal administration of neutralizing anti-IL-12 at the time of high-dose LPS challenge reduced lung IL-12, interferon-gamma, CXCL9, and CXCL10 but did not affect levels of the other chemokines or Th2-type cytokines, and did not restore AHR. These findings suggest that the amelioration of airway hyperresponsiveness observed in LPS-treated, CRAg-sensitized mice is coincident with an immune deviation of the lung inflammatory response, independent of IL-12.

L56 ANSWER 6 OF 48 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
DUPLICATE 2

ACCESSION NUMBER: 2003:587307 BIOSIS Full-text
DOCUMENT NUMBER: PREV200300570277
TITLE: Release of both CCR4-active and CXCR3-active chemokines during human allergic pulmonary late-phase reactions.
AUTHOR(S): Bochner, Bruce S. [Reprint Author]; Hudson, Sherry A.; Xiao, Hui Qing; Liu, Mark C.
CORPORATE SOURCE: Johns Hopkins Asthma and Allergy Center, 5501 Hopkins Bayview Circle, Baltimore, MD, 21224, USA
SOURCE: Journal of Allergy and Clinical Immunology, (November 2003) Vol. 112, No. 5, pp. 930-934. print.
CODEN: JACIBY. ISSN: 0091-6749.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 10 Dec 2003
Last Updated on STN: 10 Dec 2003

AB Background: Segmental antigen bronchoprovocation has long been used as a model to study allergic pulmonary inflammatory responses. Among the characteristics of the resulting cellular infiltrate is the preferential recruitment of TH2 lymphocytes. The mechanisms responsible for their selective recruitment remain unknown, but TH2 cells preferentially express the chemokine receptors CCR4 and CCR8. Objectives: We tested the hypothesis that the chemokines thymus- and activation-regulated chemokine (TARC) (CCL17) and macrophage-derived chemokine (MDC) (CCL22), whose receptor is CCR4, and I-309 (CCL1), whose receptor is CCR8, would be released at sites of segmental allergen challenge. Methods: Segmental allergen challenge with saline or allergen was performed in 10 adult allergic subjects with asthma, who were off medications. Bronchoalveolar lavage (BAL) was performed at both the saline- and allergen-challenged sites 20 hours after challenge. BAL fluids were analyzed for total cell counts and differentials, and supernatants were assayed by ELISA for levels of TARC, MDC, and I-309. As a control, the BAL fluids were also analyzed for levels of interferon- inducible protein 10 (IP-10) (CXCL10), an IFN- gamma-induced chemokine active on CXCR3, a chemokine receptor that is preferentially expressed on TH1 lymphocytes. Results: Allergen challenge led to an approximately 6-fold increase in total leukocytes, including lymphocytes, compared with those seen at saline-challenged sites. At antigen-challenged sites, eosinophils predominated. Chemokine levels at control, saline-challenged sites were either below the detectable limit or low, with the predominant chemokine detected being IP-10. At antigen-challenged sites, levels of MDC, TARC, and IP-10 were all significantly increased compared with saline sites, each with a median of 486 to 1130 pg/mL detected. On the basis

of a comparison with serum values, BAL chemokine levels at most antigen-challenged sites could not be accounted for by transudation from plasma. In contrast, levels of I-309 were extremely low or undetectable in all BAL and serum samples tested. Finally, BAL levels of MDC significantly correlated with those for TARC, but no significant correlations were found between levels of chemokine and any cell type. Conclusions: These data suggest that among the chemokines measured in this study, IP-10 is the predominant chemokine detected 20 hours after saline challenge, likely representing baseline production of a chemokine that favors TH1 cell recruitment. At antigen-challenged sites, levels of both CCR4 and CXCR3 active chemokines, but not CCR8 active chemokines, are markedly increased and are produced at levels that are likely to have biologic significance. Given the preferential accumulation of TH2 cells at these antigen-challenged sites, the increased production of CCR4-active chemokines might contribute to this response.

L56 ANSWER 7 OF 48 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:888780 CAPLUS Full-text
DOCUMENT NUMBER: 140:264545
TITLE: Effects of steroids on inflammation and cytokine gene expression in airway inflammation
AUTHOR(S): Hamid, Qutayba
CORPORATE SOURCE: Meakins-Christie Laboratory, McGill University, Montreal, QC, Can.
SOURCE: Journal of Allergy and Clinical Immunology (2003), 112(3), 636-638
CODEN: JACIBY; ISSN: 0091-6749
PUBLISHER: Mosby, Inc.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. Steroids improve airway inflammation by reducing inflammatory cell infiltrate and by promoting cellular apoptosis. In steroid-sensitive individuals, steroids reduce the number of eosinophils, mast cells, and basophils in the airway. Steroids have no or little effect on structural changes associated with airway remodeling and have no effect on reducing the subepithelial fibrosis even after prolonged treatment with inhaled steroids. They can also inhibit goblet cells hyperplasia and decrease vascularity and permeability associated with inflammation. Cytokine and chemokine genes are very sensitive to steroids.

L56 ANSWER 8 OF 48 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
DUPLICATE 3
ACCESSION NUMBER: 2003:234487 BIOSIS Full-text
DOCUMENT NUMBER: PREV200300234487
TITLE: Effect of preexposure to ultrafine carbon black on respiratory syncytial virus infection in mice.
AUTHOR(S): Lambert, Amy L. [Reprint Author]; Trasti, Frances S.; Mangum, James B.; Everitt, Jeffrey I.
CORPORATE SOURCE: Southern Research Institute, 2000 Ninth Avenue South, Birmingham, AL, 35255-5305, USA
lambert@sri.org
SOURCE: Toxicological Sciences, (April 2003) Vol. 72, No. 2, pp. 331-338. print.
ISSN: 1096-6080 (ISSN print).
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 14 May 2003
Last Updated on STN: 14 May 2003

anne.tsicopoulos@pasteur-lille.fr
SOURCE: American Journal of Respiratory and Critical Care Medicine, (July 15 2003) Vol. 168, No. 2, pp. 215-221. print.
ISSN: 1073-449X (ISSN print).
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 27 Aug 2003
Last Updated on STN: 27 Aug 2003

AB The objective of this study was to evaluate if diesel exhausts could favor helper T cell type (Th) 2-associated allergic reactions either through an increased production of Th2-associated chemokines and of their associated receptors or through a decrease of Th1-attracting chemokines and chemokine receptors. Diesel but not allergen exposure of peripheral blood mononuclear cells from subjects with allergy induced a release of I-309, whereas both diesel and Der p 1 induced an early but transient release of monokine induced by IFN-gamma and a late release of pulmonary and activation-regulated chemokine. Although both Th1- and Th2-attracting chemokines were induced, the resulting effect was an increased chemotactic activity on Th2 but not Th1 cells. Surprisingly, diesel induced a late increase in the expression of the Th1-associated CXC receptor 3 and CC receptor 5. T cell CXC receptor 3 upregulation was not associated with an increased migration to its ligands. These two antagonistic effects have been previously reported as a scavenger mechanism to clear chemokines. Altogether, these results suggest that diesel, even without allergen, may amplify a type 2 immune response but that it can also increase late Th1-associated chemokine receptor expression, perhaps as a scavenger mechanism to clear pro-Th1 chemokines and promote the Th2 pathway.

L56 ANSWER 12 OF 48 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:276192 CAPLUS Full-text
DOCUMENT NUMBER: 136:304065
TITLE: Methods and compositions for the treatment of inflammatory diseases using agents that effect glycogen synthase kinase 3β
INVENTOR(S): Pillarisetti, Sivaram; Saxena, Uday; Vines, Angela; Cahoon, Shianlen
PATENT ASSIGNEE(S): Reddy US Therapeutics, Inc., USA
SOURCE: PCT Int. Appl., 44 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002029091	A2	20020411	WO 2001-US42428	20011002
WO 2002029091	A3	20030530		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2424246	AA	20020411	CA 2001-2424246	20011002
AU 2001096959	A5	20020415	AU 2001-96959	20011002

US 2002077293	A1	20020620	US 2001-969013	20011002
US 6900041	B2	20050531		
EP 1334207	A2	20030813	EP 2001-977875	20011002

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

PRIORITY APPLN. INFO.: US 2000-237147P P 20001002
WO 2001-US42428 W 20011002

AB The present invention is directed to compns. and methods for treating inflammatory diseases comprising administration of compns. that effect glycogen synthase kinase 3β (GSK-3β) protein or gene. The present invention also comprises methods and compns. for the identification of compds. or therapeutic agents which modulate the activity of the protein. The present invention provides compns. for and methods of treatment of biol. conditions including, but not limited to, type I and type II diabetic induced vasculopathy, other vasculopathies, asthma and inflammation-induced diseases such as atherosclerosis and cell proliferation. Surprisingly, the present inventors have found that there is protective function for GSK-3β in opposing the NF-κB-induced inflammatory gene expression and that compns. and methods for increasing the GSK-3β activity are useful for treatment of inflammatory diseases, preconditions and related conditions and pathologies.

L56 ANSWER 13 OF 48 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:220631 CAPLUS Full-text
DOCUMENT NUMBER: 136:257279
TITLE: Peptide antagonist of multiple chemokine receptors and uses thereof
INVENTOR(S): Clark-Lewis, Ian; Gong, Jiang-Hong; Loetscher, Pius
PATENT ASSIGNEE(S): University of British Columbia, Can.
SOURCE: PCT Int. Appl., 55 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002022657	A2	20020321	WO 2001-CA1265	20010912
WO 2002022657	A3	20021003		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

AU 2001087463	A5	20020326	AU 2001-87463	20010912

PRIORITY APPLN. INFO.: CA 2000-2318006 A 20000912
WO 2001-CA1265 W 20010912

OTHER SOURCE(S): MARPAT 136:257279

AB The present invention provides a peptide, with the following structure, having antagonist activity toward multiple chemokine receptors: NH2-F P M F K R G R - X wherein X is: C; K; a covalent linker; C --- C R G R K F M P F - NH2, wherein C --- C represents a disulfide bridge; K - R G R K F M P F - NH2, wherein K - R represents an amide bond between the ε-amino group of K and the carboxyl group of R; or a covalent linker addnl. bound to a second NH2 - F P M

F K R G R at its C- terminal R, and wherein NH2 represents the N-terminus. The present invention also teaches methods for the production and testing of the peptide antagonist, in addition to methods of chemical modifying the peptide to enhance bioavailability and/or activity. Also provided is a therapeutic method comprising administration of the peptide antagonist to a patient in need of a reduction of chemokine receptor(s) function in the treatment of inflammatory diseases or disorders or for the prevention or reduction of HIV infection.

L56 ANSWER 14 OF 48 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN DUPLICATE 5

ACCESSION NUMBER: 2002:467986 BIOSIS Full-text
DOCUMENT NUMBER: PREV200200467986
TITLE: 2'-5' Oligoadenylate synthetase plays a critical role in interferon-gamma inhibition of respiratory syncytial virus infection of human epithelial cells.
AUTHOR(S): Behera, Aruna K.; Kumar, Mukesh; Lockey, Richard F.; Mohapatra, Shyam S. [Reprint author]
CORPORATE SOURCE: Dept. of Internal Medicine, Division of Allergy and Immunology, University of South Florida and Veterans Affairs Hospital, 13000 Bruce B. Downs Blvd., Tampa, FL, 33612, USA
smohapat@hsc.usf.edu
SOURCE: Journal of Biological Chemistry, (July 12, 2002) Vol. 277, No. 28, pp. 25601-25608. print.
CODEN: JBCHA3. ISSN: 0021-9258.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 4 Sep 2002
Last Updated on STN: 4 Sep 2002

AB Respiratory syncytial virus (RSV), associated with bronchiolitis and asthma, is resistant to the antiviral effects of type-I interferons (IFN), but not IFN-gamma . However, the antiviral mechanism of IFN-gamma action against RSV infection is unknown. The molecular mechanism of IFN-gamma-induced antiviral activity was examined in this study using human epithelial cell lines HEp-2 and A549. Exposure of these cells to 100-1000 units/ml of IFN-gamma, either before or after RSV infection, results in a significant decrease in RSV infection. After 1 h of exposure, IFN-gamma induces protein expression of IFN regulatory factor-1 (IRF-1) but not IRF-2, double-stranded RNA-activated protein kinase, and inducible nitric-oxide synthase in these cells. The mRNA for IRF-1, p40, and p69 isoforms of 2'-5' oligoadenylate synthetase (2-5 AS) are detectable, respectively, at 1 and 4 h of IFN-gamma exposure. Studies using cycloheximide and antisense oligonucleotides to IRF-1 indicate a direct role of IRF-1 in activating 2-5 AS. Cells transfected with 2-5 AS antisense oligonucleotides inhibit the antiviral effect of IFN-gamma. A stable cell line of HEp-2 overexpressing RNase L inhibitor, RLI-14, which exhibits an IFN-gamma-induced gene expression pattern similar to that of the parent cell line, shows a significant reduction in RNase L activity and IFN-gamma-mediated antiviral effect, compared with HEp-2 cells. These results provide direct evidence of the involvement of 2-5 AS in IFN-gamma-mediated antiviral activity in these cells.

L56 ANSWER 15 OF 48 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2002:955034 CAPLUS Full-text
DOCUMENT NUMBER: 138:54423
TITLE: Differential role of IFN-γ-inducible protein 10 kDa in a cockroach antigen-induced model of allergic airway

hyperreactivity: Systemic versus local effects

AUTHOR(S): Thomas, Molly S.; Kunkel, Steven L.; Lukacs, Nicholas W.

CORPORATE SOURCE: Department of Pathology, University of Michigan, Ann Arbor, MI, 48109, USA

SOURCE: Journal of Immunology (2002), 169(12), 7045-7053
CODEN: JOIMA3; ISSN: 0022-1767

PUBLISHER: American Association of Immunologists

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The ability of interferon-γ (IFN-. gamma.) to antagonize established Th2 type allergic responses is well documented. To investigate the role of IFN-.gamma .-inducible protein 10 kDa (IP10) in the allergic response, we chose to investigate the effect of IP10 neutralization on an established Th2 response. Systemic neutralization of IP10 at the time of allergen challenge increased airway hyperreactivity as well as airway eosinophil accumulation. Interestingly, IFN-γ levels were markedly reduced in both the lung and peripheral lymph node following IP10 neutralization. Furthermore, the number of CXCR3+CD4+ T cells was decreased in the peripheral lymph node following neutralization of IP10. Introduction of exogenous IP10 into the airway at the time of allergen challenge also dramatically increased eosinophil accumulation in the airway. Protein levels of IL-4, IL-5, and IL-13 were significantly increased in the lung following exogenous airway administration of IP10 with allergen. Interestingly, airway hyperreactivity was significantly decreased at early time points following concurrent IP10 and allergen challenge but rebounded at 24 and 48 h post allergen challenge. Although IP10 may initially be acting locally to dampen the allergic response, its ability to recruit eosinophils may ultimately supersede any immunomodulatory effect it may have in an established allergic response. These results suggest that while systemic levels of IP10 are beneficial in controlling the allergic response, possibly by regulating cellular trafficking in the lymph node, local administration of exogenous IP10 into an established allergic response may be detrimental.

REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L56 ANSWER 16 OF 48 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2002:414870 CAPLUS Full-text

DOCUMENT NUMBER: 137:62062

TITLE: Diesel exposure favors Th2 cell recruitment by mononuclear cells and alveolar macrophages from allergic patients by differentially regulating macrophage-derived chemokine and IFN-γ-induced protein-10 production

AUTHOR(S): Fahy, Olivier; Senechal, Stephanie; Pene, Jerome; Scherpereel, Arnaud; Lassalle, Philippe; Tonnel, Andre-Bernard; Yssel, Hans; Wallaert, Benoit; Tsicopoulos, Anne

CORPORATE SOURCE: Institut National de la Sante et de la Recherche Medicale Unite 416, Institut Pasteur de Lille, Lille, 59 019, Fr.

SOURCE: Journal of Immunology (2002), 168(11), 5912-5919
CODEN: JOIMA3; ISSN: 0022-1767

PUBLISHER: American Association of Immunologists

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Diesel exhausts and their associated organic compds. may be involved in the recent increase in the prevalence of allergic disorders, through their ability to favor a type 2 immune response. Type 2 T cells have been shown to be

preferentially recruited by the chemokines eotaxin (CCL11), macrophage-derived chemokine (MDC, CCL22), and thymus activation-regulated chemokine (CCL17) through their interaction with CCR3 and CCR4, resp., whereas type 1 T cells are mainly recruited by IFN-γ-induced protein-10 (CXCL10) through CXCR3 binding. The aim of the study was to evaluate the effect of diesel exposure on the expression of chemokines involved in type 1 and 2 T cell recruitment. PBMC and alveolar macrophages from house dust mite allergic patients were incubated with combinations of diesel exts. and Der p 1 allergen, and chemokine production was analyzed. Diesel exposure alone decreased the constitutive IP-10 production, while it further augmented allergen-induced MDC production, resulting in a significantly increased capacity to chemoattract human Th2, but not Th1 clones. Inhibition expts. with anti-type 1 or type 2 cytokine Abs as well as cytokine mRNA kinetic evaluation showed that the chemokine variations were not dependent upon IL-4, IL-13, or IFN-γ expression. In contrast, inhibition of the B7:CD28 pathway using a CTLA-4-Ig fusion protein completely inhibited diesel-dependent increase of allergen-induced MDC production This inhibition was mainly dependent upon the CD86 pathway and to a lesser extent upon the CD80 pathway. These results suggest that the exposure to diesel exhausts and allergen may likely amplify a deleterious type 2 immune response via a differential regulation of chemokine production through the CD28 pathway.

REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L56 ANSWER 17 OF 48 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN DUPLICATE 6

ACCESSION NUMBER: 2002:351463 BIOSIS Full-text
DOCUMENT NUMBER: PREV200200351463
TITLE: **IFN-gamma-inducible protein** 10 (CXCL10) contributes to airway hyperreactivity and airway inflammation in a mouse model of **asthma.**
AUTHOR(S): Medoff, Benjamin D.; Sauty, Alain; Tager, Andrew M.; MacLean, James A.; Smith, R. Neal; Mathew, Anuja; Dufour, Jennifer H.; Luster, Andrew D. [Reprint author]
CORPORATE SOURCE: Center for Immunology and Inflammatory Diseases, Division of Rheumatology, Allergy, and Immunology, Massachusetts General Hospital, 13th Street, Building 149-8301, Charlestown, MA, 02129, USA
luster@helix.mgh.harvard.edu
SOURCE: Journal of Immunology, (May 15, 2002) Vol. 168, No. 10, pp. 5278-5286. print.
CODEN: JOIMA3. ISSN: 0022-1767.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 19 Jun 2002
Last Updated on STN: 19 Jun 2002

AB Allergic **asthma** is an inflammatory disease of the airways characterized by eosinophilic inflammation and airway hyper-reactivity. Cytokines and chemokines specific for Th2-type inflammation predominate in **asthma** and in animal models of this disease. The role of Th1-type inflammatory mediators in **asthma** remains controversial. **IFN-gamma-inducible protein** 10 (IP-10; CXCL10) is an **IFN-gamma-inducible** chemokine that preferentially attracts activated Th1 lymphocytes. IP-10 is up-regulated in the airways of asthmatics, but its function in **asthma** is unclear. To investigate the role of IP-10 in allergic airway disease, we examined the expression of IP-10 in a murine model of **asthma** and the effects of overexpression and deletion of IP-10 in this model using IP-10-transgenic and IP-10-deficient mice. Our experiments demonstrate that IP-10 is up-regulated in the lung after allergen challenge. Mice that overexpress IP-10 in the lung exhibited significantly

AUTHOR(S): Michalec, Lidia; Choudhury, Barun K.; Postlethwait, Edward; Wild, James S.; Alam, Rafeul; Lett-Brown, Michael; Sur, Sanjiv [Reprint author]

CORPORATE SOURCE: Asthma and Allergic Diseases Research Center and Department of Internal Medicine, Division of Allergy and Immunology, Medical Branch, National Institutes of Health, University of Texas, Galveston, TX, 77555-0762, USA
Sasur@utmb.edu

SOURCE: Journal of Immunology, (January 15, 2002) Vol. 168, No. 2, pp. 846-852. print.
CODEN: JOIMA3. ISSN: 0022-1767.

DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 13 Nov 2002
Last Updated on STN: 13 Nov 2002

AB Oxidative stress from ozone (O3) exposure augments airway neutrophil recruitment and chemokine production. We and others have shown that severe and sudden **asthma** is associated with airway neutrophilia, and that O3 oxidative stress is likely to augment neutrophilic airway inflammation in severe **asthma**. However, very little is known about chemokines that orchestrate oxidative stress-induced neutrophilic airway inflammation in vivo. To identify these chemokines, three groups of BALB/c mice were exposed to sham air, 0.2 ppm O3, or 0.8 ppm O3 for 6 h. Compared with sham air, 0.8 ppm O3, but not 0.2 ppm O3, induced pronounced neutrophilic airway inflammation that peaked at 18 h postexposure. The 0.8 ppm O3, up-regulated lung mRNA of CXCL1,2,3 (mouse growth-related oncogene-alpha and macrophage-inflammatory **protein** -2), CXCL10 (**IFN-gamma-inducible protein**-10), CCL3 (macrophage-inflammatory **protein** -1alpha), CCL7 (monocyte chemoattractant **protein**-3), and CCL11 (eotaxin) at 0 h postexposure, and expression of CXCL10, CCL3, and CCL7 mRNA was sustained 18 h postexposure. O3 increased lung **protein** levels of CXCL10, CCL7, and CCR3 (CCL7R). The airway epithelium was identified as a source of CCL7. The role of up-regulated chemokines was determined by administering control IgG or IgG Abs against six murine chemokines before O3 exposure. As expected, anti-mouse growth-related oncogene-alpha inhibited neutrophil recruitment. Surprisingly, Abs to CCL7 and CXCL10 also decreased neutrophil recruitment by 63 and 72%, respectively. These findings indicate that CCL7 and CXCL10, two chemokines not previously reported to orchestrate neutrophilic inflammation, play a critical role in mediating oxidative stress-induced neutrophilic airway inflammation. These observations may have relevance in induction of neutrophilia in severe **asthma**.

L56 ANSWER 20 OF 48 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN DUPLICATE 9

ACCESSION NUMBER: 2002:484004 BIOSIS Full-text
DOCUMENT NUMBER: PREV200200484004

TITLE: Long-term inhalation of diesel exhaust affects cytokine expression in murine lung tissues: Comparison between low- and high-dose diesel exhaust exposure.

AUTHOR(S): Saito, Yoshinobu; Azuma, Arata; Kudo, Shoji; Takizawa, Hajime; Sugawara, Isamu [Reprint author]

CORPORATE SOURCE: Department of Molecular Pathology, The Research Institute of Tuberculosis, 3-1-24 Matsuyama, Kiyose, Tokyo, 204-0022, Japan
sugawara@jata.or.jp

SOURCE: Experimental Lung Research, (September, 2002) Vol. 28, No. 6, pp. 493-506. print.
CODEN: EXLRDA. ISSN: 0190-2148.

DOCUMENT TYPE: Article
LANGUAGE: English

ENTRY DATE: Entered STN: 11 Sep 2002
Last Updated on STN: 11 Sep 2002

AB The authors investigated the effect of diesel exhaust (DE) on cytokine expression in murine lung tissues. BALB/c mice were exposed to DE for 1 month at different dose levels of DE (low dose: diesel exhaust particles (DEP) 100mug/m3; high dose: 3 mg/m3). After exposure, the authors examined mRNA expression of cytokines (tumor nocrosis factor alpha (TFN-alpha), Interleukin (IL)-1beta, IL-4, IL-6, IL-10, IL-12p40, and interferon gamma (IFN-gamma) and inducible nitric oxide synthase (iNOS) in the lung, and also measured the secretion of TNF-alpha and IL-10 protein by alveolar macrophages (AM). The mRNA expression levels of inflammatory cytokines (TNF-alpha, IL-1beta, IL-6, IL-12p40, IFN- gamma) and iNOS, which are important for host defense, were suppressed significantly. However, the IL-10 mRNA level was increased by DE exposure. The IL-4 mRNA level was increased by low-dose DE exposure but suppressed by high-dose DE exposure. TNF-alpha and IL-10 secretion by AM paralleled mRNA expression. Chronic inhalation of DE affects cytokine expression in murine lung. These results suggest that DE alters immunological responses in the lung and may increase susceptibility to pathogens, and that increased IL-4 expression by low-dose DE exposure may induce allergic reaction such as asthma.

L56 ANSWER 21 OF 48 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN

ACCESSION NUMBER: 2002:353869 BIOSIS Full-text
DOCUMENT NUMBER: PREV200200353869
TITLE: CXC chemokine receptor-2 is necessary for the development and persistence of chronic fungal asthma in mice.
AUTHOR(S): Schuh, Jane M. [Reprint author]; Blease, Kate; Hogaboam, Cory M.
CORPORATE SOURCE: Medical School, University of Michigan, 1301 Catherine Road, Ann Arbor, MI, 48109-0602, USA
SOURCE: FASEB Journal, (March 20, 2002) Vol. 16, No. 4, pp. A331. print.
Meeting Info.: Annual Meeting of the Professional Research Scientists on Experimental Biology. New Orleans, Louisiana, USA. April 20-24, 2002.
CODEN: FAJOEC. ISSN: 0892-6638.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 26 Jun 2002
Last Updated on STN: 26 Jun 2002

AB The role of CXCR2 during Aspergillus fumigatus-induced asthma was addressed. CXCR2-deficient mice (CXCR2-/-) and controls (CXCR2+/+) were sensitized to A. fumigatus antigens and challenged with A. fumigatus conidia. The resulting allergic airway disease was followed for 37 days. At days 3 and 7 after conidia, CXCR2-/- mice had increased airway hyperreactivity (AHR) compared with CXCR2+/+ mice. In contrast, CXCR2-/- mice revealed less AHR than controls at days 14 and 37 after conidia. At all times after conidia, IL-4, IL-5, and eotaxin/CCL11 levels were significantly reduced in CXCR2-/- lungs compared with controls. Eosinophil and T cell, but not neutrophil, recruitment into the airways of sensitized CXCR2-/- mice was impaired at all times after conidia challenge compared with controls. IFN-gamma, IP-10/CXCL10, and MIG/CXC19 were increased in CXCR2-/- lungs compared with CXCR2+/+ lungs at various times after conidia. Interestingly, the early neutrophil recruitment and airway hyperresponsiveness in CXCR2-/- mice was mediated by IP-10/CXCL10 and MIG/CXCL9. Taken together, these data suggest that CXCR2 contributes to the persistence of asthmatic disease due to A. fumigatus.

L56 ANSWER 22 OF 48 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN DUPLICATE 10

ACCESSION NUMBER: 2002:447850 BIOSIS Full-text
DOCUMENT NUMBER: PREV200200447850
TITLE: Treatment of established asthma in a murine model using CpG oligodeoxynucleotides.
AUTHOR(S): Kline, Joel N. [Reprint author]; Kitagaki, Kunihiko; Businga, Thomas R.; Jain, Vipul V.
CORPORATE SOURCE: Univ. of Iowa Hospitals and Clinics, 200 Newton Rd., C33GH, Iowa City, IA, 52242, USA
joel-kline@uiowa.edu
SOURCE: American Journal of Physiology, (July, 2002) Vol. 283, No. 1 Part 1, pp. L170-L179. print.
CODEN: AJPHAP. ISSN: 0002-9513.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 21 Aug 2002
Last Updated on STN: 21 Aug 2002

AB Allergen immunotherapy is an effective but underutilized treatment for atopic asthma. We have previously demonstrated that CpG oligodeoxynucleotides (CpG ODN) can prevent the development of a murine model of asthma. In the current study, we evaluated the role of CpG ODN in the treatment of established eosinophilic airway inflammation and bronchial hyperreactivity in a murine model of asthma. In this model, mice with established ovalbumin (OVA)-induced airway disease were given a course of immunotherapy (using low doses of OVA) in the presence or absence of CpG ODN. All mice then were rechallenged with experimental allergen. Untreated mice developed marked airway eosinophilia and bronchial hyperresponsiveness, which were significantly reduced by treatment with OVA and CpG. CpG ODN leads to induction of antigen-induced Th1 cytokine responses; successful therapy was associated with induction of the chemokines interferon-gamma- inducible protein-10 and RANTES and suppression of eotaxin. Unlike previous studies, these data demonstrate that the combination of CpG ODN and allergen can effectively reverse established atopic eosinophilic airway disease, at least partially through redirecting a Th2 to a Th1 response.

L56 ANSWER 23 OF 48 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN DUPLICATE 11

ACCESSION NUMBER: 2002:258953 BIOSIS Full-text
DOCUMENT NUMBER: PREV200200258953
TITLE: Expression and regulation of inducible nitric oxide synthase from human primary airway epithelial cells.
AUTHOR(S): Donnelly, Louise E. [Reprint author]; Barnes, Peter J.
CORPORATE SOURCE: Department of Thoracic Medicine, Imperial College School of Medicine, National Heart and Lung Institute, Dovehouse Street, London, SW3 6LY, UK
l.donnelly@ic.ac.uk
SOURCE: American Journal of Respiratory Cell and Molecular Biology, (January, 2002) Vol. 26, No. 1, pp. 144-151. print.
CODEN: AJRBEL. ISSN: 1044-1549.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 24 Apr 2002
Last Updated on STN: 24 Apr 2002

AB Elevated levels of exhaled nitric oxide are seen in inflammatory airway diseases such as asthma, but the cellular source remains unknown. This study investigated whether human airway epithelial cells express inducible nitric oxide synthase (iNOS). Human bronchial epithelial cells stimulated with 50

ng/ml interkleukin-1beta, tumor necrosis factor-alpha, and interferon-gamma express iNOS mRNA, protein and increased nitrite in the cell culture media, which was inhibited by the selective iNOS inhibitor 1400W. Cells derived from subjects with asthma produced less nitrite than cells from normal subjects (6.59+-0.99 muM nitrite, n=15 versus 3.89+-0.42 muM nitrite, n=20; P<0.05). This was not attributed to steroid treatment of subjects with asthma because there was no difference in the amount of nitrite released from steroid-naive and steroid-treated cells (3.51+-0.46 versus 4.27+-0.7 muM nitrite, n=10). Neither dexamethasone nor budesonide inhibited iNOS mRNA induction, protein expression, or nitrite accumulation. The cells were not steroid insensitive because steroids inhibited GM-CSF release. Therefore, although these cells express iNOS under inflammatory conditions, they do not appear to be regulated directly by glucocorticosteroids.

L56 ANSWER 24 OF 48 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 2002331511 EMBASE Full-text
TITLE: A comparison of office-based physician visits for irritable bowel syndrome and for migraine and asthma.
AUTHOR: Kozma C.M.; Barghout V.; Slaton T.; Frech F.; Reeder C.E.
CORPORATE SOURCE: Dr. C.M. Kozma, Strat. Outcomes Serv. CareSci., Inc., 112 Fox Hollow Circle, West Columbia, SC 29170, United States. ckozma@carescience.com
SOURCE: Managed Care Interface, (2002) Vol. 15, No. 9, pp. 40-43+49.
Refs: 19
ISSN: 1096-5645 CODEN: MCIACK
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 006 Internal Medicine
017 Public Health, Social Medicine and Epidemiology
036 Health Policy, Economics and Management
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20021003
Last Updated on STN: 20021003

AB Three years of data from the National Ambulatory Medical Care Survey were analyzed to assess resource utilization for patients with irritable bowel syndrome (IBS), asthma, and migraine. Adjusted for prevalence, IBS-related physician visits occurred at approximately the same rate as those for asthma and 2.6 times the rate of visits for migraine. Specialist consultations for IBS were of similar frequency to those for migraine and more frequent than those for asthma. Diagnostic and screening tests were ordered more often during IBS-related visits than during mig raine-or asthma-related visits. Prescription rates were similar for all three conditions. In terms of resource consumption, this chronic disorder places a burden on patients that is comparable with that.

L56 ANSWER 25 OF 48 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN

ACCESSION NUMBER: 2002:322630 BIOSIS Full-text
DOCUMENT NUMBER: PREV200200322630
TITLE: Early high expression of IP-10 and Mx1 in F344 rats resistant to Sendai virus-induced airway injury.
AUTHOR(S): Cai, Xuezhong [Reprint author]; Castleman, William L. [Reprint author]
CORPORATE SOURCE: Pathobiology, University of Florida, 2015 SW 16th Avenue, Building 1017, Gainesville, FL, 32610-0880, USA

SOURCE: FASEB Journal, (March 20, 2002) Vol. 16, No. 4, pp. A15. print.
Meeting Info.: Annual Meeting of the Professional Research Scientists on Experimental Biology. New Orleans, Louisiana, USA. April 20-24, 2002.
CODEN: FAJOEC. ISSN: 0892-6638.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 5 Jun 2002
Last Updated on STN: 5 Jun 2002

AB BN and F344 rats differ markedly in their susceptibility to asthma -like disease induced by Sendai virus infection. Early gene expression that controls differences in susceptibility of two rat strains is still not clear. We combined suppressive subtractive hybridization and cDNA library array hybridization to identify the genes differentially expressed in BN and F344 rats at the first three days following virus inoculation. The selected clones were further verified by quantitative RT-PCR and northern blot analysis. Virus-induced genes included interferon regulatory factor 7, best5, rat RNA helicase induced by virus, guanylate-binding protein 2 (GBP-2), Mx1 and Interferon-g inducible protein 10 (IP-10). IP-10, Mx1 and GBP-2 mRNA abundance in infected F344 rats was 201.5%, 188.2% and 281.7% higher, respectively, to that in infected BN rats at 2 days post-inoculation. In situ hybridization study indicated that airway epithelial cells are the major cellular source of IP-10. IP-10 and Mx1 gene high expression in F344 rats could contribute to their resistance to virus-induced asthma-like syndrome.

L56 ANSWER 26 OF 48 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:338762 CAPLUS Full-text
DOCUMENT NUMBER: 134:362292
TITLE: Methods of determining individual hypersensitivity to a pharmaceutical agent from gene expression profile
INVENTOR(S): Farr, Spencer
PATENT ASSIGNEE(S): Phase-1 Molecular Toxicology, USA
SOURCE: PCT Int. Appl., 222 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001032928	A2	20010510	WO 2000-US30474	20001103
WO 2001032928	A3	20020725		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 1999-165398P P 19991105
US 2000-196571P P 20000411

AB The invention discloses methods, gene databases, gene arrays, protein arrays, and devices that may be used to determine the hypersensitivity of individuals to a given agent, such as drug or other chemical, in order to prevent toxic

side effects. In one embodiment, methods of identifying hypersensitivity in a subject by obtaining a gene expression profile of multiple genes associated with hypersensitivity of the subject suspected to be hypersensitive, and identifying in the gene expression profile of the subject a pattern of gene expression of the genes associated with hypersensitivity are disclosed. The gene expression profile of the subject may be compared with the gene expression profile of a normal individual and a hypersensitive individual. The gene expression profile of the subject that is obtained may comprise a profile of levels of mRNA or cDNA. The gene expression profile may be obtained by using an array of nucleic acid probes for the plurality of genes associated with hypersensitivity. The expression of the genes predetd. to be associated with hypersensitivity is directly related to prevention or repair of toxic damage at the tissue, organ or system level. Gene databases arrays and apparatus useful for identifying hypersensitivity in a subject are also disclosed.

L56 ANSWER 27 OF 48 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN DUPLICATE 12

ACCESSION NUMBER: 2001156247 EMBASE Full-text
TITLE: Stimulatory effects of B7-related protein-1 on cellular and humoral immune responses in mice.
AUTHOR: Guo J.; Stolina M.; Bready J.V.; Yin S.; Horan T.; Yoshinaga S.K.; Senaldi G.
CORPORATE SOURCE: Dr. G. Senaldi, Amgen Inc., Amgen Center M/S 15-2-B, 1 Amgen Center Drive, Thousand Oaks, CA 91320, United States. gsenaldi@amgen.com
SOURCE: Journal of Immunology, (1 May 2001) Vol. 166, No. 9, pp. 5578-5584.
Refs: 46
ISSN: 0022-1767 CODEN: JOIMA3
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 026 Immunology, Serology and Transplantation
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20010517
Last Updated on STN: 20010517

AB **Inducible** costimulator (ICOS) and B7-related **protein-1** (B7RP-1) constitute a receptor-ligand pair involved in T cell costimulation. In this study, the stimulatory effects of B7RP-1 on cellular and humoral immune responses were investigated giving mice a construct with the extracellular domain of murine B7RP-1 fused with human IgG1 Fc (B7RP-1-Fc). B7RP-1-Fc stimulated contact hypersensitivity (CH) given near either the time of sensitization or challenge with oxazolone. When given near challenge time, B7RP-1-Fc stimulated CH more than a construct containing the extracellular domain of murine B7.2 and Fc (B7.2-Fc). B7RP-1-Fc increased the number of cells in lymph nodes draining the skin sensitized with oxazolone, especially activated T cells. B7RP-1-Fc also increased the ability of the cells in these lymph nodes to induce CH when transfused into naive mice. B7RP-1-Fc stimulated the production of anti-keyhole limpet hemocyanin (KLH) Ab, increasing anti-KLH IgG, IgG2a, and IgE, whereas B7.2-Fc did not affect this production. B7RP-1-Fc also increased the number of cells in lymph nodes draining the skin immunized with KLH and their production of **IFN-. gamma.**, IL-4, and IL-10 in response to KLH. Finally, B7RP-1-Fc increased the presence of eosinophils in the bronchoalveolar lavage and lungs of mice sensitized and challenged with OVA so to mount an asthmatic reaction. B7RP-1-Fc stimulates both cellular and humoral immune responses in vivo by increasing number and function of T and B cells reacting to Ag exposure.

L56 ANSWER 28 OF 48 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:695138 CAPLUS Full-text
DOCUMENT NUMBER: 135:370528
TITLE: Cutting edge: altered pulmonary eosinophilic inflammation in mice deficient for Clara cell secretory 10-kDa protein
AUTHOR(S): Chen, Li-Chen; Zhang, Zhongjian; Myers, Allen C.; Huang, Shau-Ku
CORPORATE SOURCE: Johns Hopkins Asthma and Allergy Center, Johns Hopkins University School of Medicine, Baltimore, MD, 21224, USA
SOURCE: Journal of Immunology (2001), 167(6), 3025-3028
CODEN: JOIMA3; ISSN: 0022-1767
PUBLISHER: American Association of Immunologists
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Clara cell secretory protein (CC10) is a steroid- inducible protein, and its in vivo function is currently unclear. The role of CC10 in modulation of pulmonary allergic inflammation was examined in mice deficient for the CC10 gene. Wild-type and homozygous CC10-deficient mice were sensitized with an antigen, (Ag) OVA, and challenged with either OVA or saline. When compared with that seen in wild-type mice, a higher level of pulmonary eosinophilia was found in Ag-sensitized and challenged CC10-deficient mice. Increased levels of Th2 cytokines IL-4, IL-5, IL-9, and IL-13 were also found in CC10-deficient mice. In addition, an increased level of eotaxin, but not RANTES, was also seen in CC10-deficient mice. No difference was observed in the level of a Th1 cytokine, IFN-γ, between different groups of mice. These results provide the first in vivo evidence that CC10 plays a role in the modulation of pulmonary allergic inflammation.
REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L56 ANSWER 29 OF 48 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:125217 CAPLUS Full-text
DOCUMENT NUMBER: 134:279384
TITLE: Expression of the Th1 chemokine IFN-. gamma.-inducible protein 10 in the airway alters mucosal allergic sensitization in mice
AUTHOR(S): Wiley, Ryan E.; Palmer, Kay; Gajewska, Beata U.; Stampfli, Martin R.; Alvarez, David; Coyle, Anthony J.; Gutierrez-Ramos, Jose-Carlos; Jordana, Manel
CORPORATE SOURCE: Department of Pathology and Molecular Medicine and Division of Respiratory Diseases and Allergy, Centre for Gene Therapeutics, McMaster University, Hamilton, ON, L8N 3Z5, Can.
SOURCE: Journal of Immunology (2001), 166(4), 2750-2759
CODEN: JOIMA3; ISSN: 0022-1767
PUBLISHER: American Association of Immunologists
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Although the preliminary characterization of chemokines and their receptors has been prolific, comparatively little is known about the role of chemokines in the evolution of immune responses. The authors speculate that the preferential recruitment of a particular immune cell population has implications for the short- and long-term features of an adaptive response. To test this hypothesis, the authors employed adenovirus-mediated gene transfer to express the Th1-affiliated, CXC chemokine IFN-γ-inducible

protein (IP) 10 in the airways of mice undergoing a mucosal sensitization regimen known to result in a Th2-polarized allergic response. This resulted in a .apprx.60-75% inhibition of eosinophils in the bronchoalveolar lavage (BAL); these inflammatory changes were accompanied by enhanced IFN-γ, ablated IL-4, and, peculiarly, unaltered IL-5 and eotaxin levels in the BAL. The effect of IP-10 expression was shown to be dependent on IFN-. gamma., as there was no statistically significant reduction in BAL eosinophilia in IFN-γ knockout mice subjected to the IP-10 intervention. Flow cytometric anal. of mononuclear cells in the lung revealed a .apprx.60% reduction in the fraction of CD4+ cells expressing T1/ST2, a putative Th2 marker, and a parallel increase in the proportion expressing intracellular IFN-γ following IP-10 treatment. The effect of IP-10 expression at the time of initial Ag encounter is persistent, as mice rechallenged with OVA following the resolution of acute inflammation exhibited reduced eosinophilia and IL-4 in the BAL. Collectively, these data illustrate that local expression of the chemokine IP-10 can introduce Th1 phenomena to a Th2-predisposed context and subvert the development of a Th2 response.

REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L56 ANSWER 30 OF 48 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2001:920020 CAPLUS Full-text

DOCUMENT NUMBER: 136:182393

TITLE: Histamine regulates cytokine production in maturing dendritic cells, resulting in altered T cell polarization

AUTHOR(S): Mazzoni, Alessandra; Young, Howard A.; Spitzer, Jessica H.; Visintin, Alberto; Segal, David M.

CORPORATE SOURCE: Experimental Immunology Branch, National Cancer Institute, Bethesda, MD, USA

SOURCE: Journal of Clinical Investigation (2001), 108(12), 1865-1873
CODEN: JCINAO; ISSN: 0021-9738

PUBLISHER: American Society for Clinical Investigation

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Atopic diseases such as allergy and asthma are characterized by increases in Th2 cells and serum IgE antibodies. The binding of allergens to IgE on mast cells triggers the release of several mediators, of which histamine is the most prevalent. Here we show that histamine, together with a maturation signal, acts directly upon immature dendritic cells (iDCs), profoundly altering their T cell polarizing capacity. We demonstrate that iDCs express two active histamine receptors, H1 and H2. Histamine did not significantly affect the LPS-driven maturation of iDCs with regard to phenotypic changes or capacity to prime naive T cells, but it dramatically altered the repertoire of cytokines and chemokines secreted by mature DCs. In particular, histamine, acting upon the H2 receptor for a short period of time, increased IL-10 production and reduced IL-12 secretion. As a result, histamine-matured DCs polarized naive CD4+ T cells toward a Th2 phenotype, as compared with DCs that had matured in the absence of histamine. We propose that the Th2 cells favor IgE production, leading to increased histamine secretion by mast cells, thus creating a pos. feedback loop that could contribute to the severity of atopic diseases.

REFERENCE COUNT: 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L56 ANSWER 31 OF 48 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN DUPLICATE 13

ACCESSION NUMBER: 2001:223634 BIOSIS Full-text

Materials and Methods: Human umbilical cord mononuclear cells were isolated from umbilical cord blood cells and cultured in vitro in presence of interleukin-3 and interleukin-5. Superoxide generation was monitored with dihydrorhodamine-123, NO release was estimated by measuring the accumulation of nitrite. Expression of NO synthases proteins was detected by immunoblotting. Results: Both N-formyl-L-Methionyl-L-Leucyl-L-Phenylalanine, and 1-O-Alkyl-2-acetyl-sn-glyceryl-3-phosphoryl-choline induced superoxide release in umbilical cord eosinophils, while no response was observed with lipopolysaccharide, interleukin-4 and/or interferon- gamma. Furthermore, upon activation with different inflammatory stimuli, neither induction of nitric oxide synthesis nor expression of the constitutive and/or inducible nitric oxide synthase were observed in these eosinophils derived in vitro. Conclusion: Human umbilical cord derived eosinophils are able to produce superoxide as peripheral blood eosinophils. Whether human peripheral eosinophils are capable of NO synthesis is still the subject of considerable debate, nevertheless, our results suggest that these in vitro derived eosinophils are not capable of nitric oxide synthesis.

L56 ANSWER 33 OF 48 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:233671 CAPLUS Full-text
DOCUMENT NUMBER: 135:18488
TITLE: Granulocyte macrophage colony-stimulating factor and interleukin-5 activate STAT5 and induce CIS1 mRNA in human peripheral blood eosinophils
AUTHOR(S): Bhattacharya, Saswati; Stout, Barbara A.; Bates, Mary Ellen; Bertics, Paul J.; Malter, James S.
CORPORATE SOURCE: Departments of Pathology and Laboratory Medicine, University of Wisconsin Medical School, Madison, WI, USA
SOURCE: American Journal of Respiratory Cell and Molecular Biology (2001), 24(3), 312-316
CODEN: AJRBEL; ISSN: 1044-1549
PUBLISHER: American Thoracic Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Here, the authors examined signaling via the transcription factor STAT5 in human peripheral blood eosinophils after treatment with granulocyte macrophage colony-stimulating factor (GM-CSF) or interleukin (IL)-5. In response to either cytokine, STAT5 was rapidly tyrosine phosphorylated and acquired interferon γ activation site (GAS) DNA binding activity. Tyrosine-phosphorylated STAT5 was associated with both cytosolic and nuclear cell fractions. Consistent with activation, the transcription of a STAT5-dependent gene, cytokine inducible, SH2-containing protein (CIS1), was enhanced after cytokine stimulation. This is the first report of IL-5 regulation of CIS1 gene expression in any cell type. Given its role in cytokine signaling, CIS1 upregulation may serve to attenuate IL-5 and GM-CSF modulation of eosinophil function. Thus, active nuclear STAT5 participates in the regulation of IL-5 and GM-CSF-inducible genes in stimulated human peripheral blood eosinophils.
REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L56 ANSWER 34 OF 48 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN DUPLICATE 15
ACCESSION NUMBER: 2001:209315 BIOSIS Full-text
DOCUMENT NUMBER: PREV200100209315
TITLE: Expression of heme oxygenase in human airway epithelial cells.
AUTHOR(S): Donnelly, Louise E. [Reprint author]; Barnes, Peter J.
CORPORATE SOURCE: Dept. of Thoracic Medicine, Imperial College School of

Science, Technology and Medicine, National Heart and Lung Institute, Dovehouse Street, London, SW3 6LY, UK
l.donnelly@ic.ac.uk
SOURCE: American Journal of Respiratory Cell and Molecular Biology, (March, 2001) Vol. 24, No. 3, pp. 295-303. print.
CODEN: AJRBEL. ISSN: 1044-1549.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 2 May 2001
Last Updated on STN: 18 Feb 2002

AB Elevated levels of carbon monoxide (CO) are found in the exhaled breath of patients with inflammatory disease such as asthma and cystic fibrosis. Endogenous CO is derived from heme oxygenase (HO) (EC 1.14.99.3), which catabolizes heme-producing CO and biliverdin. There are three isoforms of HO: HO-1 is inducible by inflammatory cytokines and oxidants, including nitric oxide (NO), whereas HO-2 and HO-3 are expressed constitutively. Primary airway epithelial cells were treated with either 50 ng/ml interleukin-1beta, tumor necrosis factor-alpha, and interferon-gamma (cytomix), or the NO donor NOC-18 for up to 24 h. Cytomix-induced HO-1 expression peaked at 4 h, returning to baseline by 24 h, whereas HO-2 expression remained unchanged. This increase in HO-1 expression could not be explained by an increase in NO production as inducible NO synthase expression increased between 12 and 24 h. However, the NO donor NOC-18 (500 muM) increased HO-1 expression twofold and HO activity 25-fold, whereas cytomix treatment increased HO activity eightfold. NO induction of HO-1 was not mediated via quanylyl cyclase and was not attenuated by 1 muM dexamethasone, although dexamethasone increased HO-2 protein. Therefore, airway epithelial cells express HO-2 and can express HO-1; thus, the epithelium may be a source of increased CO in airway diseases.

L56 ANSWER 35 OF 48 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:493573 CAPLUS Full-text
DOCUMENT NUMBER: 133:134180
TITLE: Compounds and methods to inhibit or augment an inflammatory response
INVENTOR(S): Grainger, David J.; Tatalick, Lauren Marie
PATENT ASSIGNEE(S): Neorx Corporation, USA
SOURCE: PCT Int. Appl., 387 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000042071	A2	20000720	WO 2000-US821	20000112
WO 2000042071	A3	20010531		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2363067	AA	20000720	CA 2000-2363067	20000112
EP 1141011	A2	20011010	EP 2000-904325	20000112
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,				

IE, SI, LT, LV, FI, RO

JP 2005506947	T2	20050310	JP 2000-593637		20000112
PRIORITY APPLN. INFO.:			US 1999-229071	A	19990112
			US 1999-271192	A	19990317
			US 1999-452406	A	19991201
			WO 2000-US821	W	20000112

OTHER SOURCE(S): MARPAT 133:134180

AB Isolated and purified chemokine peptides, variants, and derivs. thereof, as well as chemokine peptide analogs, are provided. The chemokine peptide 3 derivs. are useful for preventing or treating diseases associated with recruitment of hematopoietic cells, and histamine release from basophils or mast cells; stroke; vascular disease (e.g. coronary artery disease, myocardial infarction, unstable angina pectoris, atherosclerosis or vasculitis); low bone mineral d.; autoimmune diseases; tumor; psoriasis; wound healing; asthma; organ transplant rejection; rheumatoid arthritis; allergy; inhibition of antigen-induced recall response; lentivirus infection or HIV infection; and parasitic or malaria infection.

L56 ANSWER 36 OF 48 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2000:84648 CAPLUS Full-text
DOCUMENT NUMBER: 132:141941
TITLE: Conjugates and fusion proteins for treating secondary tissue damage and other inflammatory conditions and disorders
INVENTOR(S): Mcdonald, John R.; Coggins, Philip J.
PATENT ASSIGNEE(S): Osprey Pharmaceuticals Limited, Can.
SOURCE: PCT Int. Appl., 204 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000004926	A2	20000203	WO 1999-CA659	19990721
WO 2000004926	A3	20001102		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2335105	AA	20000203	CA 1999-2335105	19990721
AU 9948918	A1	20000214	AU 1999-48918	19990721
EP 1098664	A2	20010516	EP 1999-932572	19990721
EP 1098664	B1	20030806		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002521019	T2	20020716	JP 2000-560919	19990721
AT 246517	E	20030815	AT 1999-932572	19990721
EP 1346731	A1	20030924	EP 2003-76150	19990721
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
ES 2205849	T3	20040501	ES 1999-932572	19990721
US 2002168370	A1	20021114	US 2001-792793	20010222

HK 1037133	A1	20031107	HK 2001-107546		20011030
US 2003215421	A1	20031120	US 2003-375209		20030224
PRIORITY APPLN. INFO.:			US 1998-120523	A2	19980722
			US 1998-155186P	P	19980722
			EP 1999-932572	A3	19990721
			WO 1999-CA659	W	19990721
			US 1999-360242	A3	19990722
			US 1999-453851	A3	19991202
			US 2001-792793	A1	20010222

AB Conjugates containing as a ligand a chemokine receptor-targeting agent, such as chemokines, and a targeted agent, such as a toxin are provided. These conjugates are used to treat inflammatory responses associated with activation, proliferation and migration of immune effector cells, including leukocyte cell types, neutrophils, macrophages, and eosinophils. The conjugates provided herein are used to lessen or inhibit these processes to prevent or at least lessen the resulting secondary effects. In particular, the conjugates are used to target toxins to receptors on secondary tissue damage-promoting cells. The ligand moiety can be selected to deliver the cell toxin to such secondary tissue damage-promoting cells as mononuclear phagocytes, leukocytes, natural killer cells, dendritic cells, and T and B lymphocytes, thereby suppressing the proliferation, migration, or physiol. activity of such cells. Among preferred conjugates are fusion proteins having a chemokine, or a biol. active fragment thereof, as the ligand moiety linked to a cell toxin via a peptide linker of from 2 to about 60 amino acid residues.

L56 ANSWER 37 OF 48 EMBASE

ACCESSION NUMBER:	2000274844 EMBASE Full-text
TITLE:	Airway remodeling is absent in CCR1(-/-) mice during chronic fungal allergic airway disease.
AUTHOR:	Blease K.; Mehrad B.; Standiford T.J.; Lukacs N.W.; Kunkel S.L.; Chensue S.W.; Lu B.; Gerard C.J.; Hogaboam C.M.
CORPORATE SOURCE:	Dr. C.M. Hogaboam, Department of Pathology, Univ. of Michigan Medical School, 1301 Catherine Road, Ann Arbor, MI 48109-0602, United States. hogaboam@path.med.umich.edu
SOURCE:	Journal of Immunology, (1 Aug 2000) Vol. 165, No. 3, pp. 1564-1572. Refs: 47 ISSN: 0022-1767 CODEN: JOIMA3
COUNTRY:	United States
DOCUMENT TYPE:	Journal; Article
FILE SEGMENT:	015 Chest Diseases, Thoracic Surgery and Tuberculosis 026 Immunology, Serology and Transplantation
LANGUAGE:	English
SUMMARY LANGUAGE:	English
ENTRY DATE:	Entered STN: 20000824 Last Updated on STN: 20000824

AB Asthmatic-like reactions characterized by elevated IgE, Th2 cytokines, C-C chemokines, eosinophilic inflammation, and persistent airway hyperresponsiveness follow pulmonary exposure to the spores or conidia from Aspergillus fumigatus fungus in sensitized individuals. In addition to these features, subepithelial fibrosis and goblet cell hyperplasia characterizes fungal-induced allergic airway disease in mice. Because lung concentrations of macrophage inflammatory protein-1α and RANTES were significantly elevated after A. fumigatus-sensitized mice received an intrapulmonary challenge with A. fumigatus spores or conidia, the present study addressed the role of their receptor, C-C chemokine receptor 1 (CCR1), in this model. A. fumigatus-sensitized CCR1 wild-type (+/+) and CCR1 knockout (-/-) mice exhibited similar increases in serum IgE and polymorphonuclear leukocyte numbers in the

bronchoalveolar lavage. Airway hyperresponsiveness was prominent in both groups of mice at 30 days after an intrapulmonary challenge with A. fumigatus spores or conidia. However, whole lung levels of IFN-γ were significantly higher whereas IL-4, IL-13, and Th2-inducible chemokines such as C10, eotaxin, and macrophage-derived chemokine were significantly lower in whole lung samples from CCR1(-/-) mice compared with CCR1(+/+) mice at 30 days after the conidia challenge. Likewise, significantly fewer goblet cells and less subepithelial fibrosis were observed around large airways in CCR1(-/-) mice at the same time after the conidia challenge. Thus, these findings demonstrate that CCR1 is a major contributor to the airway remodeling responses that arise from A. fumigatus-induced allergic airway disease.

L56 ANSWER 38 OF 48 EMBASE

ACCESSION NUMBER: 2000274839 EMBASE Full-text
TITLE: Inducible nitric oxide synthase inhibitors suppress airway inflammation in mice through down-regulation of chemokine expression.
AUTHOR: Trifilieff A.; Fujitani Y.; Mentz F.; Dugas B.; Fuentes M.; Bertrand C.
CORPORATE SOURCE: Dr. A. Trifilieff, Novartis Horsham Research Centre, Wimblehurst Road, Horsham RH12 5AB, United States. alexandre.trifilieff@pharma.novartis.com
SOURCE: Journal of Immunology, (1 Aug 2000) Vol. 165, No. 3, pp. 1526-1533.
Refs: 53
ISSN: 0022-1767 CODEN: JOIMA3
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 026 Immunology, Serology and Transplantation
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20000824
Last Updated on STN: 20000824

AB Growing evidence demonstrates that inducible NO synthase (iNOS) is induced in the airways of asthmatic patients. However, the precise role of NO in the lung inflammation is unknown. This study investigated the effect of both selective and nonselective iNOS inhibitors in an allergen-driven murine lung inflammation model. OVA challenge resulted in an accumulation of eosinophils and neutrophils in the airways. Expression of iNOS immunostaining in lung sections together with an increase in calcium-independent NOS activity in lung homogenates was also observed after OVA challenge. Treatment with iNOS inhibitors from the day of challenge to the day of sacrifice resulted in an inhibition of the inflammatory cell influx together with a down-regulation of macrophage inflammatory protein-2 and monocyte chemoattractant protein-1 production. In contrast, eosinophilic and neutrophilic inhibition was not observed with treatment during the sensitization. Both treatments induced an increased production of Th2-type cytokines (IL-4 and IL-5) with a concomitant decrease in production of Th1- type cytokine (IFN-γ). In vitro exposure of primary cultures of murine lung fibroblasts to a NO donor, hydroxylamine, induced a dose-dependent release of macrophage inflammatory protein-2 and monocyte chemoattractant protein-1. Our results suggest that lung inflammation after allergen challenge in mice is partially dependent on NO produced mainly by iNOS. NO appears to increase lung chemokine expression and, thereby, to facilitate influx of inflammatory cells into the airways.

L56 ANSWER 39 OF 48 BIOSIS DUPLICATE 16

ACCESSION NUMBER: 2000:534419 BIOSIS Full-text
DOCUMENT NUMBER: PREV200000534419
TITLE: Inducible lung-specific expression of RANTES: Preferential recruitment of neutrophils.
AUTHOR(S): Pan, Zhong-Zong; Parkyn, Lisa; Ray, Anuradha; Ray, Prabir [Reprint author]
CORPORATE SOURCE: Dept. of Internal Medicine, Pulmonary and Critical Care Section, Yale Univ. School of Medicine, 333 Cedar St., LCI 105, New Haven, CT, 06520: Prabir.Ray@yale.edu, USA
SOURCE: American Journal of Physiology, (October, 2000) Vol. 279, No. 4 Part 1, pp. L658-L666. print.
CODEN: AJPHAP. ISSN: 0002-9513.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 13 Dec 2000
Last Updated on STN: 11 Jan 2002

AB The chemokine regulated on activation normal T cells expressed and secreted (RANTES) has been implicated in eosinophil chemotaxis in asthma and allergic diseases, which are thought to be T helper (Th) type 2-dominated diseases. However, adoptive transfer of Th1 cells in mice upregulates RANTES gene expression in the lung, and increased RANTES expression has been documented in several Th1 cell-dominated conditions that are associated with neutrophilia. The in vivo role of RANTES in the pathogenesis of disease processes is not well understood. To determine the effect of RANTES expression alone in vivo, we generated transgenic mice that overexpress RANTES specifically in the lung in an inducible fashion. The airways of the transgenic mice overexpressing RANTES displayed a significant increase in neutrophil infiltration compared with that in control mice. The increased airway neutrophilia was also evident when the transgenic mice were tested in a murine model of allergic airway inflammation. RANTES expression also induced expression of the chemokine genes macrophage inflammatory protein-2, 10-kDa interferon-gamma- inducible protein, and monocyte chemoattractant protein-1 in the lungs of the transgenic mice. Our studies highlight a hitherto unappreciated role for RANTES in neutrophil trafficking during inflammation. Thus increased RANTES expression, as observed during respiratory viral infections, may play an important role in the associated neutrophilia and exacerbations of asthma.

L56 ANSWER 40 OF 48 EMBASE
ACCESSION NUMBER: 2000412837 EMBASE Full-text
TITLE: Chemokines and chemokine receptors in pulmonary diseases.
AUTHOR: Sadikot R.T.; Christman J.W.; Blackwell T.S.
CORPORATE SOURCE: T.S. Blackwell, Center for Lung Research, Vanderbilt University, School of Medicine, Nashville, TN 37232-2650, United States. timothy.blackwell@mcmail.vanderbilt.edu
SOURCE: Current Opinion in Investigational Drugs, (2000) Vol. 1, No. 3, pp. 314-320.
Refs: 65
ISSN: 0967-8298 CODEN: CIDREE
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 015 Chest Diseases, Thoracic Surgery and Tuberculosis
030 Pharmacology
037 Drug Literature Index
005 General Pathology and Pathological Anatomy
029 Clinical Biochemistry
026 Immunology, Serology and Transplantation
016 Cancer
LANGUAGE: English

ENTRY DATE: Entered STN: 20001213
Last Updated on STN: 20001213
DATA NOT AVAILABLE FOR THIS ACCESSION NUMBER

L56 ANSWER 41 OF 48 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 2002086127 EMBASE Full-text
TITLE: Chemokines and their role in airway hyper-reactivity.
AUTHOR: Blease K.; Lukacs N.W.; Hogaboam C.M.; Kunkel S.L.
CORPORATE SOURCE: Dr. K. Blease, Department of Pathology, Univ. of Michigan Medical School, 1301 Catherine Road, Ann Arbor, MI 48109, United States. kblease@path.med.umich.edu
SOURCE: Respiratory Research, (2000) Vol. 1, No. 1, pp. 54-61.
Refs: 71
ISSN: 1465-9921
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 015 Chest Diseases, Thoracic Surgery and Tuberculosis
026 Immunology, Serology and Transplantation
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20020321
Last Updated on STN: 20020321
AB Airway hyper-reactivity is a characteristic feature of many inflammatory lung diseases and is defined as an exaggerated degree of airway narrowing. Chemokines and their receptors are involved in several pathological processes that are believed to contribute to airway hyperresponsiveness, including recruitment and activation of inflammatory cells, collagen deposition and airway wall remodeling. These proteins are therefore thought to represent important therapeutic targets in the treatment of airway hyper-responsiveness. This review highlights the processes thought to be involved in airway hyper-responsiveness in allergic asthma , and the role of chemokines in these processes. Overall, the application of chemokines to the prevention or treatment of airway hyper-reactivity has tremendous potential.

L56 ANSWER 42 OF 48 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 2000420352 EMBASE Full-text
TITLE: Inducible lung-specific expression of RANTES: Preferential recruitment of neutrophils.
AUTHOR: Pan Z.-Z.; Parkyn L.; Ray A.; Ray P.
CORPORATE SOURCE: P. Ray, Dept. of Internal Medicine, Pulmonary and Critical Care Section, Yale Univ. School of Medicine, 333 Cedar St., New Haven, CT 06520, United States. Prabir.Ray@yale.edu
SOURCE: American Journal of Physiology - Lung Cellular and Molecular Physiology, (2000) Vol. 279, No. 4 23-4, pp. L658-L666.
Refs: 56
ISSN: 1040-0605 CODEN: APLPE7
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 005 General Pathology and Pathological Anatomy
015 Chest Diseases, Thoracic Surgery and Tuberculosis
026 Immunology, Serology and Transplantation
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20001214

PUBLISHER: American Association of Immunologists
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Corneal inflammation (keratitis) is a major cause of visual impairment in Onchocerca volvulus infection. Previous studies showed that onchocercal keratitis can be induced in mice following s.c. immunization and intracorneal injection with soluble O. volvulus antigens (OvAg), and that the inflammatory response is dependent on T cells and IL-4. Since recombinant IL-12 impairs IL-4-dependent, Th2-mediated responses in other parasitic infections and in models of allergic asthma, the present study was undertaken to determine the effect of IL-12 on onchocercal keratitis. Mice were injected i.p. with IL-12 or saline at the time of initial sensitization to OvAg. Surprisingly, IL-12 treatment caused exacerbation of corneal pathol., which was associated with increased eosinophil and mononuclear cell infiltration into the corneal stroma. Consistent with the well-documented effect of IL-12 on Th1 cell development, corneas of IL-12-treated animals had elevated expression of the Th1 cytokine IFN-γ and diminished expression of the Th2 cytokines IL-4, IL-5, IL-10, and IL-13. However, corneas from these animals also had marked elevation of α- and β-chemokines known to be active on eosinophils and mononuclear cells, including IFN -γ-inducible protein (IP)-10, macrophage inflammatory protein-1α, macrophage inflammatory protein-1β, JE/monocyte chemotactic protein-1, RANTES, and eotaxin. Thus, IL-12 exacerbates OvAg-mediated corneal pathol. by enhancing chemokine expression and recruitment of inflammatory cells.

REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

ACCESSION NUMBER: 97035148 EMBASE Full-text
DOCUMENT NUMBER: 1997035148
TITLE: Prenatal allergen contact with milk proteins.
AUTHOR: Szepfalusi Z.; Nentwich I.; Gerstmayr M.; Jost E.; Todoran L.; Gratzl R.; Herkner K.; Urbanek R.
CORPORATE SOURCE: Dr. Z. Szepfalusi, Department of Pediatrics, University of Vienna-AKH, Wahringer Gurtel 18-20, A-1090 Vienna, Austria
SOURCE: Clinical and Experimental Allergy, (1997) Vol. 27, No. 1, pp. 28-35.
Refs: 28
ISSN: 0954-7894 CODEN: CLEAEN
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 007 Pediatrics and Pediatric Surgery
026 Immunology, Serology and Transplantation
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 970303
Last Updated on STN: 970303

AB Background: Cellular proliferation to various allergens (Dermatophagoides pteronyssinus, β-lactoglobulin, bovine serum albumin, ovalbumin) has been found in cord blood cells. Whether this reflects a sensitization during foetal life is uncertain. Objective: We studied the cellular reactivity and cytokine production of cord blood cells in response to cow's milk proteins in a randomly selected group of newborns. The delineation of possible in utero allergen contact was attempted. Methods: Cord blood mononuclear cells from 39 neonates were incubated with cow's milk proteins (α-lactalbumin, β-lactoglobulin, casein, α-casein, β-casein, κ-casein, bovine serum albumin) for 7 days, and proliferation was assessed by incorporation of [3H]thymidine. Cord blood cell-derived interferon-. gamma. (IFNγ) and interleukin-4 (IL-4)

=> dup rem l61
PROCESSING COMPLETED FOR L61
L62 12 DUP REM L61 (8 DUPLICATES REMOVED)

=> d 1-12 ibib abs

L62 ANSWER 1 OF 12 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:961475 CAPLUS Full-text
DOCUMENT NUMBER: 143:227950
TITLE: Cytokine inhibition of eosinophils
INVENTOR(S): Rothenberg, Marc Elliot; Fulkerson, Patricia Chandhok
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 33 pp., Cont.-in-part of U.S. Ser. No. 752,659.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005191273	A1	20050901	US 2005-91288	20050328
US 2004141951	A1	20040722	US 2004-752659	20040107
CA 2512090	AA	20040729	CA 2004-2512090	20040107
EP 1581166	A2	20051005	EP 2004-700562	20040107
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				

PRIORITY APPLN. INFO.:
US 2003-438412P P 20030107
US 2004-752659 A2 20040107
WO 2004-US199 W 20040107

AB The cytokine CXCL9 (MIG) inhibited eosinophil responses by a CCR3- and Rac2-dependent mechanism.

L62 ANSWER 2 OF 12 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:370386 CAPLUS Full-text
DOCUMENT NUMBER: 142:461989
TITLE: The carboxyl terminus of the chemokine receptor CCR3 contains distinct domains which regulate chemotactic signaling and receptor down-regulation in a ligand-dependent manner
AUTHOR(S): Sabroe, Ian; Jorritsma, Annelies; Stubbs, Victoria E. L.; Xanthou, Georgina; Jopling, Louise A.; Ponath, Paul D.; Williams, Timothy J.; Murphy, Philip M.; Pease, James E.
CORPORATE SOURCE: Leukocyte Biology Section, Biomedical Sciences Division, Imperial College London, UK
SOURCE: European Journal of Immunology (2005), 35(4), 1301-1310
CODEN: EJIMAF; ISSN: 0014-2980
PUBLISHER: Wiley-VCH Verlag GmbH & Co. KGaA
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The chemokine receptor CCR3 regulates the chemotaxis of leukocytes implicated in allergic disease, such as eosinophils. Incubation of eosinophils with CCL11, CCL13 or CCL5 resulted in a rapid decrease of cell-surface CCR3 which was replicated using CCR3 transfectants. Progressive truncation of the CCR3 C terminus by 15 amino acids produced three constructs, Δ340, Δ325 and Δ310. Δ340 And Δ325 were able to bind CCL11 with affinities similar to wild-type

CCR3. Δ340 Transfectants exhibited enhanced migration and reduced receptor down-regulation in response to CCL11 and CCL13. Δ325 Transfectants displayed chemotactic responses to CCL11 and CCL13 similar to wild-type CCR3, and had impaired down-regulation when stimulated with CCL13 but not CCL11. In contrast, neither the Δ325 nor Δ340 truncation affected chemotaxis or receptor down-regulation induced by CCL5. Δ310 Transfectants bound CCL11 poorly and were biol. inactive. Inhibitors of p38 mitogen-activated protein kinase and PI3-kinase antagonized eosinophil shape change responses and chemotaxis of transfectants to CCL11 and CCL13. In contrast, shape change but not chemotaxis was sensitive to inhibition of the extracellular signal-regulated kinase kinase pathway suggesting differential regulation of the two responses. Thus, the CCR3 C terminus contains distinct domains responsible for the regulation of receptor desensitization and for coupling to chemotactic responses.

REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L62 ANSWER 3 OF 12 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2004:589019 CAPLUS Full-text

DOCUMENT NUMBER: 141:122348

TITLE: Cytokine-containing composition and method to alter eosinophil function and recruitment

INVENTOR(S): Rothenberg, Marc Elliot; Fulkerson, Patricia Chandhok

PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 24 pp.
CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004141951	A1	20040722	US 2004-752659	20040107
CA 2512090	AA	20040729	CA 2004-2512090	20040107
WO 2004062585	A2	20040729	WO 2004-US199	20040107
WO 2004062585	A3	20041104		
W: AE, AE, AG, AL, AL, AM, AM, AM, AT, AT, AU, AU, AZ, AZ, BA, BB, BG, BG, BR, BR, BW, BY, BY, BZ, BZ, CA, CH, CN, CN, CO, CO, CR, CR, CU, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EC, EE, EE, EG, ES, ES, FI, FI, GB, GD, GE, GE, GH, GH, GH, GM, HR, HR, HU, HU, ID, IL, IN, IS, JP, JP, KE, KE, KG, KG, KP, KP, KP, KR, KR, KZ, KZ, KZ, LC, LK, LR, LS, LS, LT, LU, LV, MA, MD, MD, MG, MK, MN, MW, MX, MX, MZ				
EP 1581166	A2	20051005	EP 2004-700562	20040107
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
US 2005191273	A1	20050901	US 2005-91288	20050328

PRIORITY APPLN. INFO.:

US 2003-438412P	P	20030107
US 2004-752659	A2	20040107
WO 2004-US199	W	20040107

AB An allergen-induced chemokine with inhibitory activity on eosinophils, monokine induced by interferon γ (MIG) and/or an IFN-γ-inducible protein of 10 kDa (IP-10), is administered in a pharmaceutically acceptable dose and formulation. The composition is used for prophylaxis and therapy of diseases in which eosinophilia occurs and may be administered, for example, to patients with allergy and asthma.

integrin-mediated adhesion caused by cytokine, chemokine, and chemoattractant stimulation. Transduction of TAT-dnRas into nondividing eosinophils inhibited endogenous Ras activation and extracellular signal-regulated kinase (ERK) phosphorylation caused by IL-5, eotaxin-1, and fMLP. IL-5, eotaxin-1 , or fMLP caused 1) change of Mac-1 to its active conformation and 2) focal clustering of Mac-1 on the eosinophil surface. TAT-dnRas or PD98059, a pharmacological mitogen-activated protein/ERK kinase inhibitor, blocked both focal surface clustering of Mac-1 and the change to active conformational structure of this integrin assessed by the mAb CBRM1/5, which binds the activation epitope. Eosinophil adhesion to the endothelial ligand ICAM-1 was correspondingly blocked by TAT-dnRas and PD98059. As a further control, we used PMA, which activates ERK phosphorylation by postmembrane receptor induction of protein kinase C, a mechanism which bypasses Ras. Neither TAT-dnRas nor PD98059 blocked eosinophil adhesion to ICAM-1, up-regulation of CBRM1/5, or focal surface clustering of Mac-1 caused by PMA. In contrast to beta(2)-integrin adhesion, neither TAT-dnRas nor PD98059 blocked the eosinophil adhesion to VCAM-1. Thus, a substantially different signaling mechanism was identified for beta(1)-integrin adhesion. We conclude that H-Ras-mediated activation of ERK is critical for beta(2)-integrin adhesion and that Ras-protein functions as the common regulator for cytokine-, chemokine-, and G-protein-coupled receptors in human eosinophils.

L62 ANSWER 7 OF 12 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:670379 CAPLUS Full-text
DOCUMENT NUMBER: 137:323404
TITLE: MAPK activation is involved in posttranscriptional regulation of RSV-induced RANTES gene expression
AUTHOR(S): Pazdrak, Konrad; Olszewska-Pazdrak, Barbara; Liu, Tianshuang; Takizawa, Ryuta; Brasier, Allan R.; Garofalo, Roberto P.; Casola, Antonella
CORPORATE SOURCE: Department of Pediatrics, University of Texas Medical Branch, Galveston, TX, 77555, USA
SOURCE: American Journal of Physiology (2002), 283(2, Pt. 1), L364-L372
CODEN: AJPHAP; ISSN: 0002-9513
PUBLISHER: American Physiological Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Airway epithelial cells represent the primary cell target of respiratory syncytial virus (RSV) infection. They actively participate in the lung immune/inflammatory response that follows RSV infection by expressing chemokines, small chemotactic cytokines that recruit and activate leukocytes. Regulated on activation, normal T cell expressed, and presumably secreted (RANTES) is a member of the CC chemokine subfamily and is strongly chemotactic for T lymphocytes, monocytes, basophils, and eosinophils, cell types that are present or activated in the inflammatory infiltrate that follows RSV infection of the lung. RSV infection of airway epithelial cells induces RANTES expression by increasing gene transcription and stabilizing RNA transcripts. The signaling pathway regulating RANTES gene expression after RSV infection has not been determined In this study, we examined the role of extracellular signal-regulated kinase (ERK) and p38, members of the mitogen-activated protein (MAP) kinase (MAPK) family, in RSV-induced RANTES production RSV infection of alveolar epithelial cells induced increased phosphorylation and catalytic activity of ERK and the upstream kinases Raf-1 and MAP ERK kinase. Induction of the MAP signaling cascade required a replication-competent virus. RSV infection of alveolar epithelial cells also induced activation of p38 MAPK. Inhibition of ERK and p38 activation significantly reduced RSV-induced RANTES mRNA and protein secretion without affecting RANTES gene transcription or transcription factor activation. These results indicate that the MAPK

AB The organic compounds of diesel exhaust particles (DEP-PAHs) have been shown to favor immunoglobulin production and bronchial hyperresponsiveness and to affect cytokine and chemokine productions. To evaluate if diesel exhaust could act in synergy with a house dust mite allergen (Der p 1), peripheral blood mononuclear cells from allergic patients were exposed to DEP-PAHs, with or without purified Der p 1. DEP-PAHs and Der p 1 separately induced an increase in interleukin (IL)-8, regulated on activation, normal T cells expressed and secreted (RANTES), and tumor necrosis factor-alpha concentrations. Interestingly, a synergy between the two stimuli was also observed. In the case of monocyte chemotactic protein (MCP)-1, DEP-PAHs reduced the release, whereas Der p 1 enhanced it. A simultaneous exposure led to reduced production as compared with allergen exposure alone, but still represented an increase as compared with the control exposure. Mitogen-activated protein (MAP) kinase Erk1/2 antagonist mainly inhibited the release of MCP-1, whereas MAP kinase p38 antagonist mainly suppressed the release of IL-8 and RANTES. Messenger RNA expression correlated with protein measurements. Moreover, supernatants from cells exposed to both DEP-PAHs and Der p 1 had a significant chemotactic activity on neutrophils and eosinophils. These findings suggest that simultaneous exposure of allergic patients to DEPs and allergens could result in high local chemokine levels via MAP kinase pathways activation, increasing the likelihood of reaching a critical threshold leading to the initiation of respiratory allergic symptoms.

L62 ANSWER 11 OF 12 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1998:219233 CAPLUS Full-text
DOCUMENT NUMBER: 128:320397
TITLE: Analysis of signal transduction pathways in human eosinophils activated by chemoattractants and the T-helper 2-derived cytokines interleukin-4 and interleukin-5
AUTHOR(S): Coffer, Paul J.; Schweizer, Rene C.; Dubois, Gerald R.; Moikoe, Tjander; Lammers, Jan-Willem J.; Koenderman, Leo
CORPORATE SOURCE: Departments of Pulmonary Diseases and Dermatology/Allergology, University Hospital Utrecht, Utrecht, 3508 GA, Neth.
SOURCE: Blood (1998), 91(7), 2547-2557
CODEN: BLOOAW; ISSN: 0006-4971
PUBLISHER: W. B. Saunders Co.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Activation and recruitment of eosinophils in allergic inflammation is in part mediated by chemoattractants and T-helper 2 (Th2)-derived cytokines. However, little is known concerning the signal transduction mechanisms by which this activation occurs. We have investigated tyrosine kinase-mediated activation of phosphatidylinositol 3-kinase (PI3K) and compared this with the activation of the p21ras-ERK signaling pathway in human eosinophils. The related cytokines interleukin-3 (IL-3), IL-5, and granulocyte-macrophage colony-stimulating factor (GM-CSF), all induced PI3K activity detected in antiphosphotyrosine immunoppts. Furthermore, the chemoattractants platelet-activating factor (PAF), RANTES, and C5a were also able to induce phosphotyrosine-associated PI3K activity. Protein kinase B (PKB) is a downstream target of PI3K activation by growth factors. Induction of PKB phosphorylation in human eosinophils was transiently induced on activation with the cytokines IL-4 and IL-5, as well as the chemoattractants PAF, C5a, and RANTES showing a broad activation profile. Surprisingly, anal. of the activation of the mitogen-activated protein (MAP) kinases p44ERK1 and p42ERK2, showed that ERK2, but not ERK1, was transiently activated in human eosinophils after stimulation with IL-5 or PAF. Activation kinetics correlated with

activation of p21ras by both cytokines and chemoattractants as measured by a novel assay for guanosine triphosphate (GTP)-loading. Finally, using specific inhibitors of both the p21ras-ERK and PI3K signaling pathways, a role was demonstrated for PI3K, but not p21ras-ERK, in activation of the serum-treated zymosan (STZ)-mediated respiratory burst in IL-5 and PAF-primed eosinophils. In summary, these data show that in human eosinophils, Th2-derived cytokines differentially activate both PI3K and MAP kinase signal transduction pathways with distinct functional consequences showing complex regulation of eosinophil effector functions.

REFERENCE COUNT: 68 THERE ARE 68 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L62 ANSWER 12 OF 12 MEDLINE on STN

ACCESSION NUMBER: 96264709 MEDLINE Full-text

DOCUMENT NUMBER: PubMed ID: 8683135

TITLE: 5-Oxo-eicosatetraenoate is a broadly active, eosinophil-selective stimulus for human granulocytes.

AUTHOR: O'Flaherty J T; Kuroki M; Nixon A B; Wijkander J; Yee E; Lee S L; Smitherman P K; Wykle R L; Daniel L W

CORPORATE SOURCE: Department of Medicine, Wake Forest University Medical Center, Winston-Salem, NC 27157, USA.

CONTRACT NUMBER: AI 17287 (NIAID)
HL26257 (NHLBI)
HL27799 (NHLBI)
+

SOURCE: Journal of immunology (Baltimore, Md. : 1950), (1996 Jul 1) 157 (1) 336-42.
Journal code: 2985117R. ISSN: 0022-1767.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals

ENTRY MONTH: 199608

ENTRY DATE: Entered STN: 19960828
Last Updated on STN: 19980206
Entered Medline: 19960816

AB 5-Oxo-eicosatetraenoate (5-oxoETE) is gaining recognition as a chemotactic factor for eosinophilic (Eo) as well as neutrophilic (Neu) polymorphonuclear leukocytes. We found that the eicosanoid was far stronger than C5a, platelet-activating factor (PAF), leukotriene B4 (LTB4), or FMLP in stimulating Eo chemotaxis. Moreover, it had weak intrinsic degranulating effects on otherwise unstimulated Eo, produced prominent degranulation responses in Eo primed by granulocyte-macrophage CSF, and enhanced the Eo-degranulating potencies of PAF, C5a, LTB4, and FMLP by up to 10,000-fold. Low picomolar levels of 5-oxoETE also induced Eo to activate mitogen-activated protein kinases (MAPKs), as defined by shifts in the electrophoretic mobility and tyrosine phosphorylation of two immunodetectable proteins, p44 and p42. 5-OxoETE was > or = 100-fold weaker or unable to stimulate any of these responses in Neu. Finally, 5-oxo-15-hydroxy-ETE and 5-hydroxy-ETE activated both cell types, but were weaker than 5-oxoETE and had Eo/Neu potency ratios approaching unity. 5-OxoETE, thus, is uniquely potent and selective in promoting Eo not only to migrate, but also to release granule enzymes and activate MAPKs. By triggering MAPK activation, the eicosanoid may also influence the production of anaphylactoid lipids (e.g., PAF), arachidonic acid metabolites, and cytokines. 5-OxoETE therefore possesses a biologic profile well suited for mediating Eo-dominated allergic reactions in vivo.

```
=> s inhibit? and l30
L63        3259 FILE MEDLINE
L64        2898 FILE BIOSIS
L65        3029 FILE EMBASE
L66        3041 FILE CAPLUS

TOTAL FOR ALL FILES
L67       12227 INHIBIT? AND L30

=> s (eosinophil or granulocyte)(a)(function or recruit?)(5a)inhibit?
L68         101 FILE MEDLINE
L69         101 FILE BIOSIS
L70          97 FILE EMBASE
L71         115 FILE CAPLUS

TOTAL FOR ALL FILES
L72         414 (EOSINOPHIL OR GRANULOCYTE)(A)(FUNCTION OR RECRUIT?)(5A) INHIBIT
                ?

=> s (eosinophil or granulocyte)(a)(function or recruit?)(a)inhibit?
L73          28 FILE MEDLINE
L74          23 FILE BIOSIS
L75          25 FILE EMBASE
L76          40 FILE CAPLUS

TOTAL FOR ALL FILES
L77         116 (EOSINOPHIL OR GRANULOCYTE)(A)(FUNCTION OR RECRUIT?)(A) INHIBIT?

=> dup rem l77
PROCESSING COMPLETED FOR L77
L78          50 DUP REM L77 (66 DUPLICATES REMOVED)

=> s l77 and l5
L79           0 FILE MEDLINE
L80           0 FILE BIOSIS
L81           0 FILE EMBASE
L82           0 FILE CAPLUS

TOTAL FOR ALL FILES
L83           0 L77 AND L5

=> d 1-50 l78 ibib abs

L78  ANSWER 1 OF 50  BIOSIS  COPYRIGHT (c) 2005 The Thomson Corporation  on STN
ACCESSION NUMBER:    2005:448382  BIOSIS Full-text
DOCUMENT NUMBER:     PREV200510239869
TITLE:               Experimental study on mechanism of Taizijian II in
                     anti-recurrence of children asthma.
AUTHOR(S):           Zhao Yu-fang [Reprint Author]; Yu Jing-mao; Zhou Da-xing
CORPORATE SOURCE:    Xiamen Univ, Coll Med, Xiamen 361005, Peoples R China
SOURCE:              Xiamen Daxue Xuebao (Ziran Kexue Ban), (JUL 2005) Vol. 44,
                     No. 4, pp. 589-592.
                     ISSN: 0438-0479.
DOCUMENT TYPE:       Article
LANGUAGE:            Chinese
ENTRY DATE:          Entered STN: 3 Nov 2005
                     Last Updated on STN: 3 Nov 2005
AB    Using asthmatic model on guinea pigs in the experiment, forty guinea pigs were
      divided randomly into 5 groups as follows: normal group, model group,
      Taizijian II large dose group, Taizijian 11 small dose group and dexamethasone
```

(DXM) group. The guinea pigs of the latter 4 groups were sensitized and induced asthmatic attack repeatedly every other day for 5 times with Egg Albumin and those of normal group were done with physiological saline. At the same time, the former 2 groups were treated with physiological saline and the latter 3 groups were treated respectively with Taizijian 11 in large dose, Taizijian 11 in small dose and DXM. And then we investigated the influence of Taizijian 11 on Eosinophils count (EC) in blood and airway, Eosinophil Cationic Protein (ECP) and Interleukin-5 in blood of asthmatic guinea pigs. The result was that Taizijian 11 could decrease EC, **inhibit eosinophil recruitment** in airway and decrease Interleukin-5 and ECP in blood to relieve the airway lesions. So Taizijian 11 could relieve the chronic allergic airway inflammation in asthmatic guinea pigs and stop asthma recurrence.

L78 ANSWER 2 OF 50 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:191493 CAPLUS Full-text
TITLE: Synthesis and evaluation of 2-aza-bicyclo[2.2.2]octane-containing α4β1 integrin antagonists in animal models of asthma
AUTHOR(S): Lawson, Edward C.; Abraham, William M.; Damiano, Bruce P.; Dyatkin, Alexey B.; De Garavilla, Larry; Kinney, William A.; Maryanoff, Bruce E.; Page, Clive; Rudman, Sandra; Santulli, Rosemary
CORPORATE SOURCE: Drug Discovery, Johnson & Johnson Pharmaceutical Research & Development, Spring House, PA, 19477-0776, USA
SOURCE: Abstracts of Papers, 229th ACS National Meeting, San Diego, CA, United States, March 13-17, 2005 (2005), MEDI-160. American Chemical Society: Washington, D. C.
CODEN: 69GQMP
DOCUMENT TYPE: Conference; Meeting Abstract
LANGUAGE: English
AB The cell-surface integrin α4β1 mediates cell adhesion and activation through cell-cell and cell-matrix interactions. The synthesis and biol. activity of 1, a potent α4β1 antagonist (Ramos cell adhesion/VCAM-1 IC50 = 39 nM), will be discussed. Administration of 1 to Ascaris-sensitized sheep via inhalation inhibited cell recruitment to the lung, blocked the late phase of asthma, and abolished airway hyperreactivity at 24 h post-dosing. In ovalbumin-sensitized guinea pigs, administration of 1 (i.p.) inhibited cell recruitment to the lung and blocked airway resistance. Ester prodrugs were synthesized to improve oral bioavailability; however, the pharmacokinetic profiles in rats and dogs were not significantly changed. Interestingly, oral dosing of two different prodrugs of 1 significantly **inhibited eosinophil recruitment** to the lung (10 mg/kg) and ovalbumin-induced airway resistance (10, 30 mg/kg) in sensitized guinea pigs.

L78 ANSWER 3 OF 50 MEDLINE on STN DUPLICATE 1
ACCESSION NUMBER: 2005234463 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 15869039
TITLE: Anti-IgE and other new immunomodulation-based therapies for allergic asthma.
AUTHOR: Jonkers R E; van der Zee J S
CORPORATE SOURCE: Department of Pulmonology, Academic Medical Centre, Amsterdam, The Netherlands.. r.e.jonkers@amc.uva.nl
SOURCE: Netherlands journal of medicine, (2005 Apr) 63 (4) 121-8.
Ref: 44
Journal code: 0356133. ISSN: 0300-2977.

PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200506
ENTRY DATE: Entered STN: 20050505
Last Updated on STN: 20050622
Entered Medline: 20050621

AB Understanding of the cellular and molecular mechanisms in asthma has lead to the recognition of a number of potential therapeutic targets, a few of which have been evaluated in clinical studies. Parenteral administrations of both anti-IL-5 and IL-12 inhibit eosinophil recruitment to the airways, but display a lack of clinical efficacy. Interrupting the IL-4 pathway thus far has also shown disappointing results in clinical studies. Omalizumab is the first anti-IgE monoclonal antibody developed for the treatment of moderate to severe asthmatics to receive FDA approval. In a number of clinical trials treatment with omalizumab was associated with moderate improvements in a number of relevant endpoints, including the rate of occurrence of disease exacerbations. Newer DNA-based therapeutic strategies including DNA vaccination and the antisense oligonucleotides show promise but thus far have only been tested in animal models.

L78 ANSWER 4 OF 50 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 2004486045 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 15454120
TITLE: Concentration-dependent activity of mometasone furoate and dexamethasone on blood eosinophils isolated from atopic children: modulation of Mac-1 expression and chemotaxis.
AUTHOR: Sale Rosa; Sabatini Federica; Silvestri Michela; Serpero Laura; Petecchia Loredana; Rossi Giovanni A
CORPORATE SOURCE: Pulmonary Disease Unit, G. Gaslini Institute, Genoa, 16147 Genoa, Italy.
SOURCE: International immunopharmacology, (2004 Dec 15) 4 (13) 1687-96.
Journal code: 100965259. ISSN: 1567-5769.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200508
ENTRY DATE: Entered STN: 20040930
Last Updated on STN: 20050816
Entered Medline: 20050815

AB Treatment of asthma with corticosteroids results in downregulation of eosinophilic airway inflammation. We evaluated in vitro the activity of an "inhaled" corticosteroid, mometasone furoate (MF), and of a "systemic" corticosteroid, dexamethasone (DEX), on eosinophil functions, i.e. adhesion molecule expression and cell chemotaxis. Partially purified blood eosinophils were obtained from 18 asthmatic subjects sensitized to house dust mites. The expression of the macrophage antigen (Mac)-1 (CD11b/CD18) was measured by specific monoclonal antibody (mAb) staining and flow cytometry analysis at baseline or after stimulation with N-formyl-methionyl-leucyl-phenylalanine (fMLP) or with recombinant human (rh) granulocyte macrophage-colony stimulating factor (GM-CSF) plus a mAb anti-human (ah) IgE low affinity receptor [FcepsilonRII or CD23]. Cell chemotaxis toward the complement fragment 5a (C5a) or rh interleukin (IL)-5 was evaluated in Boyden microchambers by light microscopy. Eosinophils showed a significant increase

in Mac-1 expression after activation with fMLP or with rh GM-CSF plus ah CD23 mAbs ($p<0.05$, each comparison) and a remarkable chemotactic response to both C5a or rh IL-5 ($p<0.001$, each comparison). To test the inhibitory activity of MF and DEX on eosinophil functions, the cells were preincubated for 3 h with four concentrations (0.1, 1, 10 and 100 nM) of each of the two drugs, before being activated by fMLP or by rh GM-CSF plus ah CD23 mAbs or tested with C5a or with rh IL-5. Independently of the stimulus used, both Mac-1 expression and eosinophil migration were effectively downregulated by preincubation with MF or DEX at 1, 10 and 100 nM ($p<0.05$). The inhibitory activity on cell chemotaxis in response to both C5a or with rh IL-5 was higher for MF than DEX, but only at the highest concentration tested ($p<0.05$, each comparison). These data demonstrate that concentrations of MF similar to those obtained in vivo are highly effective in **inhibiting eosinophil functions** involved in airway inflammation.

L78 ANSWER 5 OF 50 MEDLINE on STN
ACCESSION NUMBER: 2005201892 IN-PROCESS Full-text
DOCUMENT NUMBER: PubMed ID: 15835818
TITLE: Effect of intranasal glucosteroid on the gene expression of interleukin-5 in nasal polyps.
AUTHOR: Zhang Luo; Han De-min; Zhou Bing; Fan Er-zhong; Liu Zhong-yan
CORPORATE SOURCE: Beijing Institute of Otorhinolaryngology, Department of Otorhinolaryngology, Head and Neck Surgery, Affiliated Beijing Tongren Hospital of Capital University of Medical Sciences, Beijing, China.. luozhang@trhos.com
SOURCE: Zhonghua er bi yan hou ke za zhi, (2004 Nov) 39 (11) 672-5. Journal code: 16210350R. ISSN: 0412-3948.
PUB. COUNTRY: China
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: Chinese
FILE SEGMENT: NONMEDLINE; IN-PROCESS; NONINDEXED; Priority Journals
ENTRY DATE: Entered STN: 20050420
Last Updated on STN: 20050420

AB OBJECTIVE: To investigate the effect of intranasal glucosteroid treatment on the expression of interleukin (IL)-5 gene in nasal polyps. METHODS: Nasal polyps from topical steroid treated patients (n = 20) and untreated patients (n = 20) were investigated with the technique of mRNA in situ hybridization. RESULTS: The majority of IL-5 mRNA positive cells in nasal polyps were lymphocytes or eosinophils. No statistical significance was found in the densities of IL-5 mRNA positive cells between allergic patients [(12.6 +/- 4.6)/0.25mm2] and nonallergic patients [(14.3 +/- 4.1)/0.25mm2] ($t = -0.775$, $P > 0.05$). Compared with the control group [(13.9 +/- 4.2)/0.25mm2], the density of IL-5 mRNA positive cells was decreased in the steroid-treated group [(10. 2 +/- 3.1)/0.25mm2], and the difference reached statistical significance ($t = 3.114$, $P < 0.01$). CONCLUSIONS: These findings indicate that topical steroid treatment may suppress the IL-5 gene expression, and steroids may **inhibit eosinophil functions**.

L78 ANSWER 6 OF 50 MEDLINE on STN DUPLICATE 3
ACCESSION NUMBER: 2004540697 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 15313880
TITLE: Anti-inflammatory effects of nitric oxide-releasing hydrocortisone NCX 1022, in a murine model of contact dermatitis.
AUTHOR: Hyun Eric; Bolla Manlio; Steinhoff Martin; Wallace John L; Soldato Piero Del; Vergnolle Nathalie
CORPORATE SOURCE: Mucosal Inflammation Research Group, Faculty of Medicine,

University of Calgary, Calgary, Alberta, Canada.
SOURCE: British journal of pharmacology, (2004 Nov) 143 (5) 618-25.
Electronic Publication: 2004-08-16.
Journal code: 7502536. ISSN: 0007-1188.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200504
ENTRY DATE: Entered STN: 20041030
Last Updated on STN: 20050429
Entered Medline: 20050428

AB 1 The concept that nitric oxide (NO) release can be beneficial in inflammatory conditions has raised more attention in the recent years, particularly with the development of nitric oxide-releasing anti-inflammatory drugs. There is considerable evidence that NO is capable of enhancing the anti-inflammatory benefits of conventional anti-inflammatory drugs. 2 Since hydrocortisone is the most widely used anti-inflammatory drug for the treatment of skin inflammation, we compared the anti-inflammatory effects of hydrocortisone to an NO-releasing derivative of hydrocortisone, NCX 1022, in a murine model of irritant contact dermatitis, induced by epidermal application of benzalkonium chloride. 3 Topical pre- and post-treatment with NCX 1022 (3 nmol) in C57BL6 mice not only reduced ear oedema formation in a dose-dependent manner, but also was significantly more effective than the parent compound during the initial stages of inflammation (from 1 to 5 h). NCX 1022, but not hydrocortisone, significantly inhibited granulocyte recruitment (tissue myeloperoxidase activity). Histological samples of mouse ears treated with NCX 1022 showed significant reduction in both the number of infiltrated cells and disruption of the tissue architecture compared to hydrocortisone-treated tissues. 4 With intravital microscopy, we observed that both pre- and post-treatments with NCX 1022 were more effective than hydrocortisone in terms of inhibiting benzalkonium chloride-induced leukocyte adhesion to the endothelium, without affecting the flux of rolling leukocytes or venule diameter. 5 These results suggest that by releasing NO, NCX 1022 modulates one of the early events of skin inflammation: the recruitment of leukocytes to the site of inflammation. Overall, we have shown that NO-hydrocortisone provided faster and greater protective effects, reducing major inflammatory parameters (leukocyte adhesion and recruitment, oedema formation, tissue disruption) compared to its parental compound.

L78 ANSWER 7 OF 50 MEDLINE on STN DUPLICATE 4
ACCESSION NUMBER: 2004165859 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 15060701
TITLE: Interleukin-5 mediates peritoneal eosinophilia induced by the F1 cell wall fraction of Histoplasma capsulatum.
AUTHOR: Sa-Nunes A; Medeiros A I; Faccioli L H
CORPORATE SOURCE: Departamento de Analises Clinicas, Toxicologicas e Bromatologicas, Faculdade de Ciencias Farmaceuticas de Ribeirao Preto, Universidade de Sao Paulo, Ribeirao Preto, SP, Brasil.
SOURCE: Brazilian journal of medical and biological research = Revista brasileira de pesquisas medicas e biologicas / Sociedade Brasileira de Biofisica ... [et al.], (2004 Mar) 37 (3) 343-6. Electronic Publication: 2004-03-03.
Journal code: 8112917. ISSN: 0100-879X.
PUB. COUNTRY: Brazil
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals

ENTRY MONTH: 200407
ENTRY DATE: Entered STN: 20040403
Last Updated on STN: 20040730
Entered Medline: 20040729

AB An alkali-insoluble fraction 1 (F1), which contains mainly ss-glucan isolated from the cell wall of Histoplasma capsulatum, induces eosinophil recruitment into the peritoneal cavity of mice. The present study was carried out to determine the participation of interleukin-5 (IL-5) in this process. Inbred C57BL/6 male mice weighing 15-20 g were treated ip with 100 microg of anti-IL-5 monoclonal antibody (TRFK-5, N=7) or an isotype-matched antibody (N=7), followed by 300 microg F1 in 1 ml PBS ip 24 h later. Controls (N=5) received only 1 ml PBS. Two days later, cells from the peritoneal cavity were harvested by injection of 3 ml PBS and total cell counts were determined using diluting fluid in a Neubauer chamber. Differential counts were performed using Rosenfeld-stained cytospin preparations. The F1 injection induced significant (P<0.01) leukocyte recruitment into the peritoneal cavity (8.4 x 10(6) cells/ml) when compared with PBS alone (5.5 x 10(6) cells/ml). Moreover, F1 selectively (P<0.01) induced eosinophil recruitment (1 x 10(6) cells/ml) when compared to the control group (0.07 x 10(6) cells/ml). Treatment with TRFK-5 significantly (P<0.01) inhibited eosinophil recruitment (0.18 x 10(6) cells/ml) by F1 without affecting recruitment of mononuclear cells or neutrophils. We conclude that the F1 fraction of the cell wall of H. capsulatum induces peritoneal eosinophilia by an IL-5-dependent mechanism. Depletion of this cytokine does not have effect on the recruitment of other cell types induced by F1.

L78 ANSWER 8 OF 50 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN DUPLICATE 5

ACCESSION NUMBER: 2005030928 EMBASE Full-text
TITLE: Chapter 6. Function of Siglec-8 on human eosinophils.
AUTHOR: Nutku E.; Aizawa H.; Hudson S.; Bochner B.S.
CORPORATE SOURCE: Dr. B.S. Bochner, Johns Hopkins Asthma/Allerg. Ctr., 5501 Hopkins Bayview Circle, Baltimore, MD 21224, United States. bbochner@jhmi.edu
SOURCE: Clinical and Experimental Allergy Reviews, (2004) Vol. 4, No. SUPPL. 2, pp. 76-81.
Refs: 61
ISSN: 1472-9725 CODEN: CEARC3
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 005 General Pathology and Pathological Anatomy
015 Chest Diseases, Thoracic Surgery and Tuberculosis
026 Immunology, Serology and Transplantation
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20050204
Last Updated on STN: 20050204

AB Eosinophil recruitment and activation are regarded as central to the pathophysiology of allergic diseases, including asthma. An improved understanding of the mechanisms involved in these responses is therefore of great relevance to asthma pathogenesis and the development of new therapeutics. As part of ongoing efforts to discover novel eosinophil-specific molecules, we recently cloned Siglec-8 (formerly called sialoadhesin family member-2) from a human eosinophil cDNA library. Siglecs (sialic acid binding Ig-like lectins) are a family of transmembrane, I-type lectins characterized by an N-terminal V-set Ig domain that binds sialic acid. We now know that Siglec-8 is expressed only on human eosinophils, basophils and mast cells, giving it a unique expression pattern on effector cells of allergic

disease. We have determined that in eosinophils, Siglec-8 exists in two isoforms, one of which contains two putative cytoplasmic tyrosine-based signalling motifs, including an ITIM (immunoreceptor tyrosine-based inhibitory motif) sequence. Because of the ITIM sequence, we hypothesized that Siglec-8 ligation would inhibit eosinophil functions. Initial studies found that incubation of eosinophils with Siglec-8 binding monoclonal antibodies under cross-linking conditions caused rapid and profound caspase-dependent apoptosis, and this response could not be rescued by the survival-promoting cytokine interleukin (IL)-5. In fact, IL-5 enhanced the ability of Siglec-8 cross-linking to induce eosinophil apoptosis. Activation via Siglec-8 could potentially be used to inhibit eosinophil survival in vivo, providing a novel strategy for reducing or inhibiting these cells in allergic and other diseases.

L78 ANSWER 9 OF 50 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:42286 CAPLUS Full-text
DOCUMENT NUMBER: 138:100921
TITLE: Methods for increasing in vivo efficacy of oligonucleotides and inhibiting inflammation in mammals
INVENTOR(S): Renzi, Paolo; Allam, Mustapha; Allakhverdi, Zoulfia
PATENT ASSIGNEE(S): Topigen Pharmaceutique Inc., Can.
SOURCE: PCT Int. Appl., 63 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2003004511	A2	20030116	WO 2002-CA1046		20020708
WO 2003004511	A3	20030710			
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
CA 2451738	AA	20030116	CA 2002-2451738		20020708
EP 1406667	A2	20040414	EP 2002-748499		20020708
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK					
JP 2004532900	T2	20041028	JP 2003-510677		20020708
US 2005032723	A1	20050210	US 2004-482949		20040816
PRIORITY APPLN. INFO.:			US 2001-303071P	P	20010706
			WO 2002-CA1046	W	20020708

AB The invention relates to the use of nucleotide substitutes for increasing the in vivo efficacy of nucleic acid mols. and also for inhibiting inflammation in mammals. More particularly, the present invention relates to the use of 2',6'-diaminopurine (DAP) and analogs thereof per se in anti-inflammatory compns., and also for preparing nucleic acid mols. having an increased in vivo physiol. efficiency and a reduced toxicity as compared to conventional oligos. The invention is particularly useful for the preparation of antisense oligonucleotides for treating pulmonary/respiratory diseases such as cystic

AUTHOR: Kaifi J T; Diaconu E; Pearlman E
CORPORATE SOURCE: Department of Medicine, Case Western Reserve University and University Hospitals of Cleveland, 2109 Adelbert Road, Cleveland, OH 44106, USA.
CONTRACT NUMBER: EY10320 (NEI)
EY11373 (NEI)
SOURCE: Journal of immunology (Baltimore, Md. : 1950), (2001 Jun 1) 166 (11) 6795-801.
Journal code: 2985117R. ISSN: 0022-1767.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200108
ENTRY DATE: Entered STN: 20010820
Last Updated on STN: 20010820
Entered Medline: 20010816

AB Infiltration of granulocytes into the transparent mammalian cornea can result in loss of corneal clarity and severe visual impairment. Since the cornea is an avascular tissue, recruitment of granulocytes such as neutrophils and eosinophils into the corneal stroma is initiated from peripheral (limbal) vessels. To determine the role of vascular adhesion molecules in this process, expression of platelet endothelial cell adhesion molecule 1 (PECAM-1), ICAM-1, and VCAM-1 on limbal vessels was determined in a murine model of ocular onchocerciasis in which Ags from the parasitic worm Onchocerca volvulus are injected into the corneal stroma. Expression of each of these molecules was elevated after injection of parasite Ags; however, PECAM-1 and ICAM-1 expression remained elevated from 12 h after injection until 7 days, whereas VCAM-1 expression was more transient, with peak expression at 72 h. Subconjunctival injection of Ab to PECAM-1 significantly inhibited neutrophil recruitment to the cornea compared with eyes injected with control Ab ($p = 0.012$). Consistent with this finding, corneal opacification was significantly diminished ($p < 0.0001$). There was no significant reduction in eosinophils. Conversely, subconjunctival injection of Ab to ICAM-1 did not impair neutrophil recruitment, but significantly inhibited eosinophil recruitment ($p = 0.0032$). Injection of Ab to VCAM-1 did not significantly inhibit infiltration of either cell type to the cornea. Taken together, these results demonstrate important regulatory roles for PECAM-1 and ICAM-1 in recruitment of neutrophils and eosinophils, respectively, to the cornea, and may indicate a selective approach to immune intervention.

L78 ANSWER 14 OF 50 MEDLINE on STN DUPLICATE 8
ACCESSION NUMBER: 2001277560 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 11371422
TITLE: Effects of dexamethasone on antigen-induced airway eosinophilia and M(2) receptor dysfunction.
AUTHOR: Evans C M; Jacoby D B; Fryer A D
CORPORATE SOURCE: Department of Environmental Health Sciences, Johns Hopkins School of Public Health, Johns Hopkins University, 615 North Wolfe Street, Baltimore, MD 21205, USA.
CONTRACT NUMBER: ES-03819 (NIEHS)
HL-54659 (NHLBI)
HL-55543 (NHLBI)
HL-61013 (NHLBI)
P01-HL-10342 (NHLBI)
SOURCE: American journal of respiratory and critical care medicine, (2001 May) 163 (6) 1484-92.
Journal code: 9421642. ISSN: 1073-449X.
PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200106
ENTRY DATE: Entered STN: 20010702
Last Updated on STN: 20010702
Entered Medline: 20010628

AB In antigen-challenged guinea pigs, airway hyperreactivity is due to recruitment of eosinophils to the airway nerves and dysfunction of M(2) muscarinic receptors. M(2) receptor dysfunction is caused by eosinophil major basic protein, which is an allosteric antagonist at the receptor. Because glucocorticoids inhibit airway hyperreactivity in humans and in animal models of asthma, we tested whether dexamethasone treatment (6 microg. kg(-)(1). d(-)(1) for 3 d, intraperitoneal) before antigen challenge prevents M(2) receptor dysfunction and airway hyperreactivity. Guinea pigs were sensitized to ovalbumin via intraperitoneal injections, and were challenged with ovalbumin via inhalation. Twenty-four hours later, hyperreactivity and M(2) receptor function were tested. Antigen-challenged animals were hyperreactive to vagal stimulation, and demonstrated loss of M(2) receptor function. Dexamethasone pretreatment prevented hyperreactivity and M(2) receptor dysfunction in antigen-challenged guinea pigs. Antigen challenge resulted in recruitment of eosinophils to the airways and to the airway nerves. Dexamethasone prevented recruitment of eosinophils to the airway nerves but did not affect total eosinophil influx into the airways. These results demonstrate that dexamethasone prevents antigen-induced hyperreactivity by protecting neuronal M(2) muscarinic receptors from antagonism by eosinophil major basic protein, and this protective mechanism appears to be by specifically **inhibiting eosinophil recruitment** to the airway nerves.

L78 ANSWER 15 OF 50 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:233670 CAPLUS Full-text
DOCUMENT NUMBER: 135:18487
TITLE: Inhibition of eosinophilic inflammation in allergen-challenged TNF receptor p55/p75- and TNF receptor p55-deficient mice
AUTHOR(S): Broide, David H.; Stachnick, Greg; Castaneda, Diego; Nayar, Jyothi; Sriramarao, P.
CORPORATE SOURCE: Department of Medicine, University of California, San Diego, La Jolla, CA, 92093-0635, USA
SOURCE: American Journal of Respiratory Cell and Molecular Biology (2001), 24(3), 304-311
CODEN: AJRBEL; ISSN: 1044-1549
PUBLISHER: American Thoracic Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB To determine the relative in vivo importance of tumor necrosis factor (TNF) release after allergen challenge to the subsequent endothelial adhesion and recruitment of eosinophils, we have compared eosinophil recruitment in TNF receptor p55/p75-deficient, TNF receptor p55-deficient, and control wild-type mice challenged with allergen. Bronchoalveolar lavage eosinophil recruitment in TNF receptor p55/p75-deficient and TNF receptor p55-deficient mice challenged with ovalbumin was significantly reduced compared with wild-type mice. To determine the mechanism of inhibition of eosinophil recruitment in TNF receptor-deficient mice, we used intravital microscopy to visualize the rolling and firm adhesion of fluorescently labeled mouse eosinophils in the microvasculature of the allergen-challenged mouse mesentery. Eosinophil rolling as well as eosinophil firm adhesion to endothelium were significantly inhibited in allergen-challenged TNF receptor p55/p75-deficient and TNF receptor p55-deficient mice compared with wild-type mice. Overall, these

studies demonstrate that TNF, released after allergen challenge, is important in the induction of endothelial cell adhesiveness, a prerequisite for recruitment of circulating eosinophils.

REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L78 ANSWER 16 OF 50 MEDLINE on STN
ACCESSION NUMBER: 2002018095 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 11446618
TITLE: Eosinophil trafficking in asthma.
AUTHOR: Wardlaw A J
CORPORATE SOURCE: Division of Respiratory Medicine, Leicester-Warwick Medical School, Glenfield Hospital.
SOURCE: Clinical medicine (London, England), (2001 May-Jun) 1 (3) 214-8. Ref: 27
Journal code: 101092853. ISSN: 1470-2118.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200112
ENTRY DATE: Entered STN: 20020121
Last Updated on STN: 20020121
Entered Medline: 20011204

AB Asthma is characterised by a 50-fold increase in the number of eosinophils relative to neutrophils in the bronchial mucosa. This is the result of the cumulative and sequential effects of several, approximately fourfold, increases in selective eosinophil versus neutrophil migration occurring at a number of stages in the life cycle of the eosinophil. These events, which are integrated and directed by allergen-specific T helper 2 lymphocytes through the generation of interleukin (IL)-5, IL-4 and IL-13, include: effects on the bone marrow, mediated principally by IL-5, which result in a fourfold increase in circulating eosinophils selective tethering of eosinophils to venular endothelium through the combined effects of P-selectin/P-selectin glycoprotein ligand (PSGL)-1 and very late activation antigen (VLA)-4/vascular cell adhesion molecule-1, which has the potential for an up to tenfold increase in eosinophil versus neutrophil adhesion selective chemotaxis under the influence of CC chemokines prolonged survival, again mediated by IL-5. The implications of this multistep process are that antagonists of IL-5, VLA-4, PSGL-1 and CC chemokine receptor 3, as well as IL-4 and IL-13, each have the potential markedly to inhibit eosinophil recruitment in asthma.

L78 ANSWER 17 OF 50 MEDLINE on STN DUPLICATE 9
ACCESSION NUMBER: 2001076844 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 11086084
TITLE: Eotaxin is specifically cleaved by hookworm metalloproteases preventing its action in vitro and in vivo.
AUTHOR: Culley F J; Brown A; Conroy D M; Sabroe I; Pritchard D I; Williams T J
CORPORATE SOURCE: Leukocyte Biology Section, Biomedical Sciences Division, Imperial College School of Medicine, South Kensington, London, United Kingdom.. f.culley@ic.ac.uk
SOURCE: Journal of immunology (Baltimore, Md. : 1950), (2000 Dec 1) 165 (11) 6447-53.
Journal code: 2985117R. ISSN: 0022-1767.
PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200101
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20010111

AB Eotaxin is a potent eosinophil chemoattractant that acts selectively through CCR3, which is expressed on eosinophils, basophils, mast cells, and Th2-type T cells. This arm of the immune system is believed to have evolved to control helminthic parasites. We hypothesized that helminths may employ mechanisms to **inhibit eosinophil recruitment**, to prolong worm survival in the host. We observed that the excretory/secretory products of the hookworm Necator americanus **inhibited eosinophil recruitment** in vivo in response to eotaxin, but not leukotriene B(4), a phenomenon that could be prevented by the addition of protease inhibitors. Using Western blotting, N. americanus supernatant was shown to cause rapid proteolysis of eotaxin, but not IL-8 or eotaxin-2. N. americanus homogenate was fractionated by gel filtration chromatography, and a FACS-based bioassay measured the ability of each fraction to inhibit the activity of a variety of chemokines. This resulted in two peaks of eotaxin-degrading activity, corresponding to approximately 15 and 50 kDa molecular mass. This activity was specific for eotaxin, as responses to other agonists tested were unaffected. Proteolysis of eotaxin was prevented by EDTA and phenanthroline, indicating that metalloprotease activity was involved. Production of enzymes inactivating eotaxin may be a strategy employed by helminths to prevent recruitment and activation of eosinophils at the site of infection. As such this represents a novel mechanism of regulation of chemokine function in vivo. The existence of CCR3 ligands other than eotaxin (e.g., eotaxin-2) may reflect the evolution of host counter measures to parasite defense systems.

L78 ANSWER 18 OF 50 MEDLINE on STN DUPLICATE 10
ACCESSION NUMBER: 2000428116 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 10948184
TITLE: CD4(+) depletion selectively **inhibits eosinophil recruitment** to the cornea and abrogates Onchocerca volvulus keratitis (River blindness).
AUTHOR: Hall L R; Kaifi J T; Diaconu E; Pearlman E
CORPORATE SOURCE: Department of Medicine, Division of Geographic Medicine, Case Western Reserve University and University Hospitals of Cleveland, Cleveland, Ohio 44106, USA.
CONTRACT NUMBER: EY06913 (NEI)
EY10320 (NEI)
EY11373 (NEI)
SOURCE: Infection and immunity, (2000 Sep) 68 (9) 5459-61.
Journal code: 0246127. ISSN: 0019-9567.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200009
ENTRY DATE: Entered STN: 20000922
Last Updated on STN: 20000922
Entered Medline: 20000908

AB Previous studies demonstrated that in the murine model of Onchocerca volvulus keratitis, neutrophils and eosinophils are recruited into the cornea in a biphasic manner in response to intrastromal injection. To determine if CD4(+) T cells regulate migration of neutrophils and eosinophils into the cornea, CD4(+) cells were depleted using monoclonal antibody GK1.5 before intrastromal

injection of parasite antigens. Depletion of CD4(+) cells abrogated corneal opacification at later but not early stages of disease. Consistent with this observation, CD4 depletion significantly impaired recruitment of eosinophils to the cornea but had no effect on neutrophils. These data indicate that CD4(+) T cells mediate sustained O. volvulus keratitis by regulating eosinophil recruitment to the cornea.

L78 ANSWER 19 OF 50 MEDLINE on STN DUPLICATE 11
ACCESSION NUMBER: 2000486094 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 11033768
TITLE: Mucosal IL-12 is more effective than systemic IL-12 in augmenting IFN-gamma expression and inhibiting allergic lung eosinophilia in murine lungs.
AUTHOR: Sur S; Choudhury B K; Lam J S; Bouchard P; Wild J S; Sur N; Alam R; Sigounas A; Holbert D; Van Scott M R
CORPORATE SOURCE: Department of Internal Medicine, University of Texas Medical Branch, Galveston 77555-0762, USA.. Sasur@utmb.edu
CONTRACT NUMBER: 1 KO8 AI 0153901 (NIAID)
SOURCE: Experimental lung research, (2000 Sep) 26 (6) 457-76. Journal code: 8004944. ISSN: 0190-2148.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200102
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20010201

AB The relative efficacy of mucosal (intratracheal) and systemic (intraperitoneal) delivery of interleukin (IL)-12 was evaluated in a mouse model of allergic lung eosinophilia. Mucosal administration of IL-12 achieved 100- to 600-fold higher bronchoalveolar lavage (BAL) levels of IL-12, but 2- to 10-fold lower serum levels compared to systemic administration. Whereas both mucosal and systemic IL-12 inhibited BAL eosinophil recruitment at high doses (100-1000 ng), only mucosal IL-12 was effective at low doses (1-10 ng). Mucosal, but not systemic, administration of 1000 ng of IL-12 increased interferon (IFN)-gamma expression in BAL cells. In a model of ongoing eosinophilic inflammation, when mucosal or systemic IL-12 doses were initiated prior to peak eosinophilia, further eosinophil recruitment was inhibited. However, when IL-12 treatment was initiated after peak eosinophil recruitment occurred, recovery from eosinophilic inflammation was not facilitated. Our findings are the first to demonstrate that locally administered IL-12 inhibits eosinophil recruitment at 100-fold lower doses than systemic IL-12. The most likely mechanism of this enhanced inhibitory activity is a sustained increase in lung levels of IL-12 that augments IFN-gamma production from BAL cells. We suggest that future studies should evaluate the efficacy of low doses of nebulized IL-12 in inhibiting eosinophilic lung inflammation in asthma.

L78 ANSWER 20 OF 50 MEDLINE on STN DUPLICATE 12
ACCESSION NUMBER: 2000200550 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 10734180
TITLE: SB 239063, a potent p38 MAP kinase inhibitor, reduces inflammatory cytokine production, airways eosinophil infiltration, and persistence.
AUTHOR: Underwood D C; Osborn R R; Kotzer C J; Adams J L; Lee J C; Webb E F; Carpenter D C; Bochnowicz S; Thomas H C; Hay D W; Griswold D E
CORPORATE SOURCE: Department of Pulmonary Pharmacology, SmithKline Beecham

Pharmaceuticals, King of Prussia, Pennsylvania, USA.
SOURCE: Journal of pharmacology and experimental therapeutics, (2000 Apr) 293 (1) 281-8.
Journal code: 0376362. ISSN: 0022-3565.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200004
ENTRY DATE: Entered STN: 20000505
Last Updated on STN: 20000505
Entered Medline: 20000421

AB The anti-inflammatory/antiallergic activity of a novel second-generation p38 mitogen-activated protein kinase inhibitor, SB 239063[trans-1-(4-hydroxycyclohexyl) -4-(4-fluorophenyl)-5-(2-methoxypyridimidin-4-yl)imidazole], was investigated in vivo and in vitro. SB 239063 had an IC(50) of 44 nM for inhibition of recombinant purified human p38alpha. In lipopolysaccharide-stimulated human peripheral blood monocytes, SB 239063 inhibited interleukin-1 and tumor necrosis factor-alpha production (IC(50) values = 0.12 and 0.35 microM, respectively). A role for p38 kinase in cytokine-associated inflammation in the mouse was shown by p38 activation in the lung and inhibition of lipopolysaccharide-induced tumor necrosis factor-alpha production by SB 239063 (ED(50) = 5.8 mg/kg p.o.). Antiallergic activity was demonstrated by essential abolition (approximately 93% inhibition) of inhaled ovalbumin (OA)-induced airway eosinophilia by SB 239063 (12 mg/kg p.o.), measured by bronchoalveolar lavage (BAL) in OA-sensitized mice. In addition, p38 kinase was found by Western analysis to be activated in guinea pig lung. Administration of SB 239063 (10 or 30 mg/kg p.o.) in conscious guinea pigs markedly reduced (approximately 50% inhibition) OA-induced pulmonary eosinophil influx, measured by BAL 24 h after antigen. SB 239063 (10 mg/kg b.i.d. p.o.) administered after leukotriene D(4) inhalation, reduced by 60% the persistent airway eosinophilia seen at 4 days. Apoptosis of cultured eosinophils isolated from guinea pig BAL was increased by SB 239063 (1-10 microM) in the presence of interleukin-5. These results indicate that SB 239063 is a potent inhibitor of inflammatory cytokine production, **inhibits eosinophil recruitment**, in addition to enhancing apoptosis of these cells. Collectively, the results support the potential utility of p38 kinase inhibitors, such as SB 239063, for the treatment of asthma and other inflammatory disorders.

L78 ANSWER 21 OF 50 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:417986 CAPLUS Full-text
DOCUMENT NUMBER: 131:87716
TITLE: Preparation of sulfonamides as eosinophil function inhibitors, antiallergy agents, and antiasthmatic agents
INVENTOR(S): Miyakawa, Motonori; Murai, Satoshi; Ishige, Hirohide; Suda, Masahiro; Fujimoto, Kyoko; Watanuki, Mitsuru; Nakamura, Tsutomu
PATENT ASSIGNEE(S): Kaken Pharmaceutical Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 83 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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JP 11180945 A2 19990706 JP 1997-346815 19971216
PRIORITY APPLN. INFO.: JP 1997-346815 19971216
OTHER SOURCE(S): MARPAT 131:87716
AB R1XYNR2SO2ZCONR3R4 [R1-R3 = H, C1-9 alkyl, C3-7 cycloalkyl, (un)substituted aryl, (un)substituted heterocyclyl, etc.; X = SO2NH, CONH, NHCONH, NHCSNH; Y = C1-6 alkylene, C2-6 alkenylene, C2-6 alkynylene,; Z = phenylene, heterocyclylene; R4 = H, C1-9 alkyl, sulfonyl, Ph, (un)substituted heterocyclyl, etc.], their salts, their hydrates, or their solvates are prepared Their synthetic intermediates are also claimed. 4-ClC6H4SO2NH(CH2)2NPhSO2C6H4CO2H-2 (11.8 g) was chlorinated with SOCl2 and amidated with 4.6 g Et m-aminobenzoate to give 10.7 g of the corresponding amide, which at 0.1 μM inhibited 97.9% release of eosinophil peroxidase.

L78 ANSWER 22 OF 50 MEDLINE on STN DUPLICATE 13
ACCESSION NUMBER: 1999248218 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 10229876
TITLE: Long term prevention of allergic lung inflammation in a mouse model of asthma by CpG oligodeoxynucleotides.
AUTHOR: Sur S; Wild J S; Choudhury B K; Sur N; Alam R; Klinman D M
CORPORATE SOURCE: Division of Allergy and Immunology, Department of Internal Medicine, University of Texas Medical Branch, Galveston, TX 77555, USA.. Sasur@utmb.edu
SOURCE: Journal of immunology (Baltimore, Md. : 1950), (1999 May 15) 162 (10) 6284-93.
Journal code: 2985117R. ISSN: 0022-1767.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals; AIDS
ENTRY MONTH: 199906
ENTRY DATE: Entered STN: 19990628
Last Updated on STN: 19990628
Entered Medline: 19990614
AB Asthma is an inflammatory disease of the airways that is induced by Th2 cytokines and inhibited by Th1 cytokines. Despite a steady increase in the incidence, morbidity, and mortality from asthma, no current treatment can reduce or prevent asthma for a prolonged period. We examined the ability of unmethylated CpG oligodeoxynucleotides (ODN), which are potent inducers of Th1 cytokines, to prevent the inflammatory and physiological manifestations of asthma in mice sensitized to ragweed allergen. Administration of CpG ODN 48 h before allergen challenge increased the ratio of IFN-gamma to IL-4 secreting cells, diminished allergen-induced eosinophil recruitment, and decreased the number of ragweed allergen-specific IgE-producing cells. These effects of CpG ODN were sustained for at least 6 wk after its administration. Furthermore, there was a vigorous Th1 memory response to the recall Ag, inhibition of peribronchial and perivascular lung inflammation, and inhibition of bronchial hyperresponsiveness 6 wk after administration of CpG ODN. Administration of CpG ODN in IFN-gamma -/- mice failed to inhibit eosinophil recruitment, indicating a critical role of IFN-gamma in mediating these effects. This is the first report of a treatment that inhibits allergic lung inflammation in presensitized animals for a prolonged period and thus has relevance to the development of an effective long term treatment for asthma.

L78 ANSWER 23 OF 50 MEDLINE on STN DUPLICATE 14
ACCESSION NUMBER: 2000020175 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 10550733
TITLE: Molecular basis for selective eosinophil trafficking in asthma: A multistep paradigm.

AUTHOR: Wardlaw A J
CORPORATE SOURCE: Division of Respiratory Medicine, Leicester University Medical School, Leicester, United Kingdom.
SOURCE: Journal of allergy and clinical immunology, (1999 Nov) 104 (5) 917-26. Ref: 103
Journal code: 1275002. ISSN: 0091-6749.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199912
ENTRY DATE: Entered STN: 20000113
Last Updated on STN: 20000113
Entered Medline: 19991222

AB Asthma is characterized by a 50- to 100-fold increase in the number of eosinophils relative to neutrophils in the bronchial mucosa. This increase is not the result of a single molecular event but of the cumulative and sequential effects of several approximately 4-fold increases in selective eosinophil versus neutrophil migration, occurring at a number of stages in the life cycle of the eosinophil. These steps include (1) effects on the bone marrow, mediated principally by IL-5, which result in a 4-fold increase in circulating eosinophils, (2) selective tethering of eosinophils to venular endothelium through the combined effects of P-selectin/P-selectin glycoprotein ligand 1 and very late activation antigen-4/vascular cell adhesion molecule-1, which has the potential for an up to 10-fold increase in eosinophil versus neutrophil adhesion, (3) selective chemotaxis under the influence of CC chemokines, and (4) prolonged survival, again mediated by IL-5. These events are integrated and directed by allergen-specific T(H)2 lymphocytes through the generation of IL-5, IL-4, and IL-13. The implications of this multistep process are that antagonists of IL-5, very late activation antigen-4, P-selectin glycoprotein ligand 1, and CCR3 as well as IL-4 and IL-13 each have the potential to markedly inhibit eosinophil recruitment in asthma.

L78 ANSWER 24 OF 50 MEDLINE on STN DUPLICATE 15
ACCESSION NUMBER: 1999398071 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 10469273
TITLE: Eotaxin and eotaxin receptor (CCR3) expression in Sephadex particle-induced rat lung inflammation.
AUTHOR: Harrington P M; Newton D J; Williams C M; Hunt J A; Dearman R J; Kimber I; Coleman J W; Flanagan B F
CORPORATE SOURCE: Department of Immunology, University of Liverpool, Alderley Park, Macclesfield, UK.
SOURCE: International journal of experimental pathology, (1999 Jun) 80 (3) 177-85.
Journal code: 9014042. ISSN: 0959-9673.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199912
ENTRY DATE: Entered STN: 20000113
Last Updated on STN: 20000113
Entered Medline: 19991223

AB The beta chemokine eotaxin is a potent eosinophil activator and chemoattractant. We examined immunohistochemically eotaxin protein expression in a range of normal rat tissues and in rat lung during Sephadex particle-induced pulmonary inflammation. The time course of eotaxin expression in lung at various time points after Sephadex administration was related to the

appearance of eosinophils in the bronchoalveolar lavage fluid and tissue distribution of eotaxin receptor (CCR3) positive cells. Results showed that eotaxin protein was constitutively expressed by both lung airway epithelial cells and gut epithelial cells in normal tissues in the absence of inflammation. During Sephadex induced pulmonary inflammation, eotaxin expression increased in alveolar macrophages prior to the major increase in eosinophil numbers which reached a peak at 72 h. The pattern of eotaxin pulmonary expression and the location of CCR3 receptor positive cells suggest a chemoattractant gradient resulting in migration firstly into the tissue and subsequently through the airway epithelium into the airways. Treatment of rats with the glucocorticoid dexamethasone or the immunosuppressant cyclosporin A reduced eosinophil entry into lung tissue and airways but had no apparent effect on eotaxin expression in vivo, indicating that both these drugs **inhibit eosinophil recruitment** either by an eotaxin-independent mechanism, or by targetting factors that synergise with eotaxin, or an event post eotaxin expression.

L78 ANSWER 25 OF 50 MEDLINE on STN DUPLICATE 16
ACCESSION NUMBER: 1998200591 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 9531595
TITLE: Inhibition of eosinophil rolling and recruitment in P-selectin- and intracellular adhesion molecule-1-deficient mice.
COMMENT: Erratum in: Blood 1998 Jul 1;92(1):343
AUTHOR: Broide D H; Humber D; Sullivan S; Sriramarao P
CORPORATE SOURCE: Department of Medicine, University of California, San Diego, CA, USA.
CONTRACT NUMBER: AI 33977 (NIAID)
AI 35796 (NIAID)
AI 38425 (NIAID)
SOURCE: Blood, (1998 Apr 15) 91 (8) 2847-56.
Journal code: 7603509. ISSN: 0006-4971.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199805
ENTRY DATE: Entered STN: 19980520
Last Updated on STN: 19990129
Entered Medline: 19980512

AB To determine the relative in vivo importance of endothelial expressed adhesion molecules to eosinophil rolling, adhesion, and transmigration, we have induced eosinophilic peritonitis using ragweed allergen in P-selectin-deficient, intracellular adhesion molecule-1 (ICAM-1)-deficient and control wild-type mice. Circulating leukocytes visualized by intravital microscopy exhibited reduced rolling and firm adhesion in P-selectin-deficient mice and reduced firm adhesion in ICAM-1-deficient mice. Eosinophils exhibited reduced rolling and firm adhesion to endothelium in P-selectin-deficient mice. Eosinophil recruitment in P-selectin-deficient mice (approximately 75% inhibition of eosinophil recruitment) and ICAM-1-deficient mice (approximately 67% inhibition of eosinophil recruitment) was significantly reduced compared with wild-type mice. Eosinophil recruitment was not completely inhibited in P-selectin/ICAM-1 double-mutant mice (**eosinophil recruitment inhibited** approximately 62%). However, pretreatment of P-selectin/ICAM-1-deficient mice with an anti-vascular cell adhesion molecule (VCAM) antibody induced near complete inhibition of eosinophil recruitment. Overall, these studies show that eosinophil rolling and firm adhesion is significantly reduced in P-selectin-deficient mice and that P-selectin, ICAM-1, and VCAM are important to eosinophil peritoneal recruitment after ragweed challenge.

L78 ANSWER 26 OF 50 MEDLINE on STN DUPLICATE 17
ACCESSION NUMBER: 1998391067 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 9725251
TITLE: Contribution of endothelial selectins and alpha 4 integrins to eosinophil trafficking in allergic and nonallergic inflammatory reactions in skin.
AUTHOR: Teixeira M M; Hellewell P G
CORPORATE SOURCE: Applied Pharmacology, Imperial College School of Medicine, National Heart and Lung Institute, London, United Kingdom.
SOURCE: Journal of immunology (Baltimore, Md. : 1950), (1998 Sep 1) 161 (5) 2516-23.
Journal code: 2985117R. ISSN: 0022-1767.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199809
ENTRY DATE: Entered STN: 19980917
Last Updated on STN: 19980917
Entered Medline: 19980910

AB The role of endothelial selectins in mediating eosinophil recruitment was assessed using the trafficking of 111In-labeled blood eosinophils in mouse skin. An intradermal injection of chemoattractants (leukotriene B4, macrophage inflammatory protein-1 alpha, and eotaxin) resulted in a rapid accumulation of 111In eosinophils that was reduced 49 to 91% by anti-P-selectin mAb. An anti-E-selectin mAb was ineffective, although a combined E- and P-selectin blockade resulted in >95% inhibition of all responses. The accumulation of a pulse of 111In eosinophils at sites of active cutaneous anaphylaxis (ACA) at 4 to 8 h and at 20 to 24 h after Ag challenge was completely dependent upon E- and P-selectin in combination, but not in isolation. In contrast, at 20 to 24 h after Ag challenge in a delayed-type hypersensitivity (DTH) reaction in skin, 111In eosinophil accumulation was largely independent of endothelial selectins, even when L-selectin was also blocked. An anti-alpha 4 integrin mAb significantly reduced 111In eosinophil trafficking in both allergic reactions but was slightly more effective in the DTH reaction compared with the ACA reaction. These results show that P-selectin and to a lesser extent E-selectin mediate eosinophil recruitment in skin in acute inflammatory reactions. In allergic, late-onset inflammatory reactions, neither P- nor E-selectin alone are sufficient to mediate eosinophil accumulation; when combined, they are essential for trafficking in ACA but are less important in the DTH reaction. Whether alpha 4 integrin-based strategies will be more effective than selectin-based strategies at **inhibiting eosinophil recruitment** in human disease remains to be determined.

L78 ANSWER 27 OF 50 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1998:107897 CAPLUS Full-text
DOCUMENT NUMBER: 128:191510
TITLE: Inhibition of pulmonary eosinophilia in P-selectin- and ICAM-1-deficient mice
AUTHOR(S): Broide, David H.; Sullivan, Sue; Gifford, Tim; Sriramarao, P.
CORPORATE SOURCE: Department of Medicine, University of California at San Diego, San Diego, CA, USA
SOURCE: American Journal of Respiratory Cell and Molecular Biology (1998), 18(2), 218-225
CODEN: AJRBEL; ISSN: 1044-1549
PUBLISHER: American Lung Association

DOCUMENT TYPE: Journal
LANGUAGE: English

AB Adhesion mol. expression by pulmonary endothelial cells is considered to play an important role in the recruitment of circulating leukocytes to sites of inflammation in the lung. The authors have used P-selectin- and intercellular adhesion mol. type 1 (ICAM-1)-deficient mice to determine whether these adhesion mols. are important to pulmonary eosinophil recruitment after allergen challenge. There was a significant inhibition of lung tissue eosinophil recruitment in ICAM-1-deficient mice (.apprx.84% inhibition compared to wild-type mice) and P-selectin-deficient mice (.apprx.67% inhibition compared to wild-type mice) 3 h after allergen challenge. The number of bronchoalveolar lavage (BAL) eosinophils in P-selectin-deficient and ICAM-1-deficient mice was also significantly reduced compared with wild-type mice. Levels of BAL eosinophil peroxidase (EPO) were significantly lower in ICAM-1-deficient mice (0.21 EPO units) compared with wild-type mice (3.34 EPO units). There was no significant difference in the degree of inhibition of eosinophil recruitment in ICAM-1-deficient mice at the three time points (3, 12, and 24 h) of study after allergen challenge. However, in P-selectin-deficient mice there was a decline in the degree of inhibition of eosinophil recruitment from 3 h (67% inhibition) and 12 h (72% inhibition) postchallenge, to 24 h postchallenge (38% inhibition), suggesting that other adhesion mols. may be playing a more prominent role than P-selectin at later time points. These studies suggest an important role for ICAM- I and P-selectin in eosinophil recruitment to the lung after allergen challenge.

REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L78 ANSWER 28 OF 50 MEDLINE on STN DUPLICATE 18
ACCESSION NUMBER: 97174278 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 9022012
TITLE: Blockade of CD28/B7 co-stimulation by mCTLA4-Hgamma1 inhibits antigen-induced lung eosinophilia but not Th2 cell development or recruitment in the lung.
AUTHOR: Harris N; Campbell C; Le Gros G; Ronchese F
CORPORATE SOURCE: Malaghan Institute of Medical Research, Wellington School of Medicine, New Zealand.
SOURCE: European journal of immunology, (1997 Jan) 27 (1) 155-61. Journal code: 1273201. ISSN: 0014-2980.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; AIDS
ENTRY MONTH: 199703
ENTRY DATE: Entered STN: 19970313
Last Updated on STN: 19970313
Entered Medline: 19970305

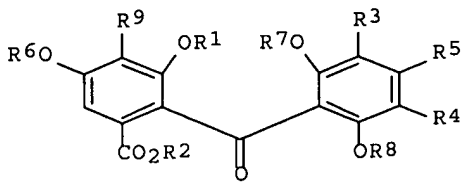
AB We have studied the role of the CD28/B7 co-stimulatory pathway in the development of a Th2-type lung immune response. Mice injected two or three times intraperitoneally with ovalbumin in alum adjuvant and then re-exposed to the same antigen by intranasal (i.n.) inoculation show infiltration of the lung tissue and appearance in the broncho-alveolar lavage (BAL) fluid of significant numbers of eosinophils and lymphocytes, in a pattern which is reminiscent of asthmatic inflammation. The accumulation of eosinophils in the airways is completely dependent on interleukin (IL)-5 secretion by CD4+ T cells. We have used mice transgenic for a soluble form of murine CTLA-4 (mCTLA4-Hgamma1) which binds to B7 molecules on antigen-presenting cells, thereby preventing their interaction with T cell-expressed CD28. mCTLA4-Hgamma1-transgenic mice immunized intraperitoneally and challenged i.n. with ovalbumin failed to generate any eosinophil infiltration, suggesting that little or no IL-5 was secreted in the lungs of these mice. In contrast with

the complete lack of eosinophils, the numbers and phenotypes of infiltrating lymphocytes were comparable in the lungs of mCTLA4-Hgamma1-transgenic and normal mice. Also, lung lymphocytes from immunized mCTLA4-Hgamma1- transgenic and normal mice could be shown to secrete comparable amounts of IL-4 and IL-5 when stimulated in culture in the absence of mCTLA4-Hgamma1. We conclude that mCTLA4-Hgamma1 can efficiently block the production of IL-5 during in vivo responses and inhibit eosinophil recruitment, but that it does not block the development of CD4+ T cells into Th2 cells with the potential to secrete IL-5.

L78 ANSWER 29 OF 50 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1996:431363 CAPLUS Full-text
DOCUMENT NUMBER: 125:86314
TITLE: Preparation of benzophenonecarboxylic acid derivatives as inhibitors of function of eosinophils
INVENTOR(S): Oohashi, Yutaka; Ishikawa, Masatoshi; Nakao, Toyoo
PATENT ASSIGNEE(S): Kirin Brewery, Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 24 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
JP 08092082	A2	19960409	JP 1995-206658		19950720
PRIORITY APPLN. INFO.:			JP 1995-206658	A	19950720
			JP 1994-168057		19940720

OTHER SOURCE(S): MARPAT 125:86314
GI



I

AB The title compds. [I; R1 = H, C1-10 alkyl; R2 = C1-12 (halo)alkyl; R3, R4 = H, halo; R5 = H, C1-10 alkyl or alkoxy; R6 - R8 = H, C1-6 alkylcarbonyl, C1-10 alkyl, OR; wherein R = 5-membered heterocyclyl containing one N atom, CHR10NH2; wherein R10 = H or C1-6 alkyl which is optionally substituted by HO, NH2, guanidino, CO2H, CONH2, SH, C1-6 alkylthio, (hydroxy)phenyl, or optionally benzene ring-condensed 5-membered heterocyclyl containing 1 or 2 N atoms], which are also useful as inhibitors of allergy, inflammation, eosinophils movement, and eosinophils degranulation, are prepared Thus, 5-benzyloxy-2-bromo-3-methoxybenzyl alc. was esterified with 2,6-dibenzyloxy-4-methylbenzoic acid using Ph3P and DEAD reagent in THF to give 5-benzyloxy-2-bromo-3-methoxybenzyl 2,6-dibenzyloxy-4-methylbenzoate, which was treated with MeLi in THF at -78°, oxidized successively with pyridinium dichromate in DMF and tetrabutylammonium permanganate in pyridine, esterified by MeI in the presence of K2CO3 in DMF, and hydrogenolyzed in the presence of Pd(OH)2 in a mixture of cyclohexene and EtOH under refluxing to give sulochrin I (R1 = R2 = R5 = Me, R3 = R4 = R6 - R9 = H). This compound at 1 μM in vitro inhibited 95%

degranulation of eosinophils preparation from human peripheral blood and at 10-5 M inhibited 82% floating of eosinophils preparation from guinea pig. It also showed IC50 of ≥30 μM against P388 mouse leukemia cells.

L78 ANSWER 30 OF 50 MEDLINE on STN DUPLICATE 19
ACCESSION NUMBER: 96290753 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 8730732
TITLE: Effects of theophylline and rolipram on antigen-induced airway responses in neonatally immunized rabbits.
AUTHOR: Gozzard N; Herd C M; Blake S M; Holbrook M; Hughes B; Higgs G A; Page C P
CORPORATE SOURCE: Department of Pharmacology, Celltech Therapeutics Ltd., Slough, Berkshire.
SOURCE: British journal of pharmacology, (1996 Apr) 117 (7) 1405-12.
Journal code: 7502536. ISSN: 0007-1188.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199610
ENTRY DATE: Entered STN: 19961022
Last Updated on STN: 20000303
Entered Medline: 19961010

AB 1. The effects of the xanthine, theophylline, a non-selective phosphodiesterase (PDE) inhibitor, and the phosphodiesterase type 4 (PDE 4) inhibitor, rolipram, were evaluated in a model of antigen-induced airway responses in the allergic rabbit. 2. Adult litter-matched NZW rabbits (2.5-3.9 kg), immunized within 24 h of birth with Alternaria tenuis antigen, were pretreated twice daily for 3 days with theophylline (3 mg kg-1, i.p) or rolipram (1 mg kg-1, i.p) prior to antigen challenge (Alternaria tenuis). For each drug-treated group, a parallel group of rabbits were pretreated with the appropriate vehicle. In all groups airway responsiveness to inhaled histamine and bronchoalveolar lavage (BAL) was performed 24 h before and after antigen-challenge. 3. Basal lung function in terms of resistance (RL, cmH2O 1(-1)s-1) and dynamic compliance (Cdyn, ml cmH2O-1) were unaltered by pretreatment with theophylline or rolipram compared to their respective vehicles 24 h prior to or post antigen challenge. 4. The acute bronchoconstriction induced by inhaled Alternaria tenuis aerosol was unaffected by pretreatment with theophylline or rolipram. 5. Airway hyperresponsiveness to inhaled histamine was indicated by reduced RL PC50 (2.4-3.5 fold) and Cdyn PC35 (2.5-2.6 fold) values 24 h after antigen challenge. Treatment with rolipram, but not theophylline, prevented the increase in responsiveness to inhaled histamine 24 h after antigen challenge. 6. Total cells per ml of BAL fluid increased 24 h after antigen challenge due to the recruitment of neutrophils and eosinophils. Antigen-induced increases in pulmonary neutrophils were unaffected; however, eosinophils were reduced 57.5% in theophylline and 82% in rolipram-treated rabbits. 7. Inhalation of Alternaria tenuis aerosol elicits an acute bronchoconstriction, followed 24 h later by an increased responsiveness to inhaled histamine and pulmonary neutrophil and eosinophil recruitment in the immunized rabbit. With the dosing regimes used, both rolipram and theophylline **inhibited eosinophil recruitment**, whilst only rolipram prevented the development of airway hyperresponsiveness. Neither agent inhibited the acute bronchoconstriction due to inhaled antigen.

L78 ANSWER 31 OF 50 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1996:292532 CAPLUS Full-text
DOCUMENT NUMBER: 125:491

TITLE: Granulocyte functions in children with cancer are differentially sensitive to the toxic effect of chemotherapy
AUTHOR(S): Lejeune, Marylene; Sariban, Eric; Cantinieaux, Brigitte; Ferster, Alina; Devalck, Christine; Fondu, Pierre
CORPORATE SOURCE: Department Haematology, Hopital Universitaire Saint-Pierre, Brussels, B-1000, Belg.
SOURCE: Pediatric Research (1996), 39(5), 835-842
CODEN: PEREBL; ISSN: 0031-3998
PUBLISHER: Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English

AB To analyze the toxicity associated to chemotherapy upon granulocytes, different functional assays were performed, within days of drug exposure and at time of bone marrow recovery, on polymorphonuclear neutrophils (PMN) from children with cancer. There were no significant postchemotherapy changes in the expression of the different receptors studied nor in the phagocytosis of Staphylococcus aureus 42D. By contrast, a significant decrease was observed in H2O2 production in PMN recently exposed to chemotherapy with both cytofluorometric and chemiluminescence assays. There was also a decrease in the production of O-2 and in chemotaxis; finally, the intracellular killing of S. aureus 42D and Escherichia coli was reduced. In patients having recovered from drug-induced bone marrow aplasia, PMN functions were normal except for bactericidal activity which was still defective. These observations indicate that, in patients exposed to chemotherapy, some PMN functions are transiently altered, whereas microorganism cell killing is continuously impaired.

L78 ANSWER 32 OF 50 MEDLINE on STN DUPLICATE 20
ACCESSION NUMBER: 97067354 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 8910767
TITLE: Lymphoblastoid interferon-alpha inhibits T cell proliferation and expression of eosinophil-activating cytokines.
AUTHOR: Krishnaswamy G; Smith J K; Srikanth S; Chi D S; Kalbfleisch J H; Huang S K
CORPORATE SOURCE: Department of Medicine, East Tennessee State University, Quillen College of Medicine, Johnson City 37614-0622, USA.
CONTRACT NUMBER: AI-340002 (NIAID)
SOURCE: Journal of interferon & cytokine research : official journal of the International Society for Interferon and Cytokine Research, (1996 Oct) 16 (10) 819-27.
Journal code: 9507088. ISSN: 1079-9907.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199703
ENTRY DATE: Entered STN: 19970327
Last Updated on STN: 19970327
Entered Medline: 19970317

AB T cell-derived cytokines, such as interleukin-5 (IL-5) and granulocyte-macrophage colony-stimulating factor (GM-CSF) activate eosinophils, whereas other cytokines, such as tumor necrosis factor (TNF)-alpha and IL-13, determine eosinophil recruitment. Interferon-alpha (IFN-alpha), a leukocyte-derived cytokine, has been shown to have beneficial effects in eosinophil-mediated disorders, such as the hypereosinophilic syndrome and a murine model of allergic asthma, where it inhibited eosinophil recruitment. We tested the hypothesis that IFN-alpha acted in eosinophil-mediated disorders by modulating

T cell cytokine expression. Peripheral blood mononuclear cells (PBMC) or human ragweed-specific TH1 (2B8) and TH2 (2D2) T cell clones were cultured in the presence of 5 micrograms/ml of phytohemagglutinin (PHA) or 25 micrograms/ml of antigen Amb a 1 (short ragweed allergen), respectively, and lymphoblastoid IFN-alpha (varying from 0 to 10,000 U/ml). We assessed T cell proliferation by [3H]thymidine incorporation and production of IL-5 and GM-CSF by ELISA. Expression of cytokine transcripts was analyzed by the reverse transcription-polymerase chain reaction technique (RT-PCR). IFN-alpha induced a dose-dependent suppression of T cell proliferation of both PBMC ($p < 0.001$) and the T cell clones ($p < 0.001$). IFN-alpha inhibited gene expression of IL-5, GM-CSF, TNF-alpha, and IL-13 in PBMC. Furthermore, IFN-alpha significantly inhibited mitogen-induced and antigen-induced production of IL-5 and GM-CSF. IFN-alpha may benefit eosinophil-mediated disorders by inhibiting T cell function and production of cytokines active on human eosinophils.

L78 ANSWER 33 OF 50 MEDLINE on STN DUPLICATE 21
ACCESSION NUMBER: 95291600 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 7539697
TITLE: Differential effects of non-selective and selective phosphodiesterase inhibitors on human eosinophil functions.
AUTHOR: Hatzelmann A; Tenor H; Schudt C
CORPORATE SOURCE: Byk Gulden, Department of Biochemistry, Konstanz, Germany.
SOURCE: British journal of pharmacology, (1995 Feb) 114 (4) 821-31. Journal code: 7502536. ISSN: 0007-1188.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199507
ENTRY DATE: Entered STN: 19950720
Last Updated on STN: 20020420
Entered Medline: 19950711

AB 1. The effect of non-selective (3-isobutyl-1-methylxanthine, IBMX; theophylline) and type IV- or type III/IV-selective (rolipram, RP 73401; zardaverine, tolafentrine) phosphodiesterase (PDE) inhibitors on human eosinophil functions was investigated. 2. For this purpose human eosinophils were purified from blood of healthy donors by a magnetic cell separation (MACS) technique to a purity > or = 99%. From the stimuli investigated (complement C5a; N-formyl-methionyl-leucyl-phenylalanine, fMLP; platelet activating factor, PAF; opsonized zymosan) C5a was selected to test the influence of the above mentioned compounds on secretion of granule constituents (eosinophil cationic protein, ECP; eosinophil-derived neurotoxin, EDN) as well as on formation of reactive oxygen species measured by luminol-enhanced chemiluminescence in intact cells. For comparison, inhibition of PDE IV activity in the cytosol of disrupted cells, which contains about 75% of total PDE IV activity, was determined. 3. Both theophylline and IBMX inhibited the two cell responses with IC50 values which were in the range of their IC50 values obtained for inhibition of PDE IV activity in the cell-free system. The beta 2-adrenoceptor agonist, salbutamol (1 mumol l-1), which by itself did not substantially influence the two cell responses, only marginally improved the potency of theophylline and IBMX in inhibiting ECP/EDN secretion. Only the IC50 value of IBMX for inhibition of chemiluminescence was lowered by about one order of magnitude in the presence of salbutamol. 4. In contrast, none of the selective PDE inhibitors tested substantially inhibited the two cell responses at concentrations up to 10 mumol l-1. This was surprising because all of the compounds investigated inhibited PDE IV activity in the cell-free system with IC50 values which were at least 30 fold lower than the highest concentration of the compounds used with intact cells. In combination with salbutamol, however, both ECP/EDN secretion and chemiluminescence was

inhibited by rolipram and zardaverine with IC50 values similar to the IC50 values for inhibition of PDE IV activity. Although RP 73401 and tolafentrine also inhibited both cell responses in the presence of salbutamol, the potency of these two compounds in **inhibiting eosinophil function** in intact cells was at least two orders of magnitude lower than would have been expected from the inhibition of PDE IV activity in the cell-free system.(ABSTRACT TRUNCATED AT 400 WORDS)

L78 ANSWER 34 OF 50 MEDLINE on STN DUPLICATE 22
ACCESSION NUMBER: 95271482 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 7752069
TITLE: The ability of phosphodiesterase IV inhibitors to suppress superoxide production in guinea pig eosinophils is correlated with inhibition of phosphodiesterase IV catalytic activity.
AUTHOR: Barnette M S; Manning C D; Cieslinski L B; Burman M; Christensen S B; Torphy T J
CORPORATE SOURCE: Department of Inflammation & Respiratory Pharmacology, SmithKline Beecham Pharmaceuticals, King of Prussia, Pennsylvania, USA.
SOURCE: Journal of pharmacology and experimental therapeutics, (1995 May) 273 (2) 674-9.
Journal code: 0376362. ISSN: 0022-3565.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199506
ENTRY DATE: Entered STN: 19950629
Last Updated on STN: 20000303
Entered Medline: 19950619

AB Elevation of cyclic AMP (cAMP) content **inhibits eosinophil function.** Because phosphodiesterase IV (PDE IV) appears to be the major PDE isozyme present in eosinophils, inhibitors of this isozyme should suppress eosinophil activation. Previous studies on PDE IV have revealed that this enzyme possesses both cAMP catalytic activity that is inhibitable by rolipram, a prototypical PDE IV inhibitor, and a high-affinity binding site for rolipram. The function of this high-affinity rolipram binding site relative to the inhibitory action of compounds is not clear because the rank order potency of PDE IV inhibitors for competing with [3H]-rolipram binding is distinct from that for inhibiting cAMP hydrolysis. Consequently, the present experiments were carried out to fulfill the following objectives: 1) to determine whether PDE IV inhibitors suppress eosinophil function and, if so, 2) to establish a correlation between this functional activity and inhibition of PDE IV catalytic activity or interaction with the high-affinity rolipram binding site. Various PDE inhibitors produced approximately 60% maximal inhibition of formylmethionine-leucine-phenylalanine-induced superoxide anion production, so that IC30 concentrations were used as a basis to compare the potency of various PDE inhibitors. Selective PDE IV inhibitors were the most potent compounds tested. PDE inhibitors selective for other isozymes were devoid of activity or considerably less potent.(ABSTRACT TRUNCATED AT 250 WORDS)

L78 ANSWER 35 OF 50 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1996:82442 CAPLUS Full-text
DOCUMENT NUMBER: 124:193357
TITLE: The influence of trimethoprim on chemiluminescence of peripheral granulocytes - experimental studies
AUTHOR(S): Wulf, Barbara; Wulf, Eberhardt

CORPORATE SOURCE: Inst. Immunol., Militaermed. Akad., Bach Saarow, Germany
SOURCE: Mikrooekologie und Therapie (1995), 21, 286-9
CODEN: MITHE4; ISSN: 0720-0536
PUBLISHER: Institut fuer Mikrooekologie
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Trimethoprim inhibited the chemiluminescence of human peripheral granulocytes, indicating a reduction of the oxidative killing capacity (respiratory burst) of the cells. An intracellular mechanism of this depression of granulocytic function by trimethoprim is concluded. An extracellular scavenger action was excluded.

L78 ANSWER 36 OF 50 MEDLINE on STN DUPLICATE 23
ACCESSION NUMBER: 94275030 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 8006305
TITLE: Glucocorticoids suppressed production and gene expression of interleukin-5 by peripheral blood mononuclear cells in atopic patients and normal subjects.
AUTHOR: Okayama H; Fushimi T; Shimura S; Sasaki H; Shirato K
CORPORATE SOURCE: First Department of Internal Medicine, Tohoku University School of Medicine, Sendai, Japan.
SOURCE: Journal of allergy and clinical immunology, (1994 Jun) 93 (6) 1006-12.
Journal code: 1275002. ISSN: 0091-6749.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199407
ENTRY DATE: Entered STN: 19940729
Last Updated on STN: 19940729
Entered Medline: 19940715

AB BACKGROUND: Interleukin-5 (IL-5) is known to play a major role in regulating eosinophil function in atopic diseases, including bronchial asthma. Glucocorticoids are most effective agents for treating these diseases. However, their mechanism remains unclear. We examined the effects of glucocorticoids on the production and gene expression of IL-5 in atopic patients and normal subjects. METHODS: Human peripheral blood mononuclear cells (PBMCs) in five atopic and four normal subjects were cultured with phytohemagglutinin and phorbol 12-myristate 13-acetate (PMA) in the presence of dexamethasone. IL-5 secreted by PBMCs was assayed by ELISA. Gene expression of IL-5 by PBMCs was assessed semiquantitatively by sequential reverse transcription-polymerase chain reaction, and Southern blot analysis. RESULTS: Phytohemagglutinin/PMA-stimulated PBMCs from all atopic patients and three normal subjects secreted detectable amounts of IL-5, which were suppressed by dexamethasone in a dose-dependent manner, with 85.8% suppression at 10(-6) mol/L. Gene expression of IL-5 was detected by reverse-transcription polymerase chain reaction in PBMCs from all subjects, even when not stimulated; was increased by stimulation; and was suppressed by dexamethasone. The concentration of dexamethasone resulting in 50% inhibition in IL-5 gene expression did not differ between atopic patients and normal subjects. CONCLUSION: These findings indicate that dexamethasone suppressed IL-5 production in atopic human PBMCs through an inhibitory action on the gene expression. These results suggest that the suppression of IL-5 production through the suppression of IL-5 gene expression is one of the most important mechanisms by which glucocorticoids inhibit eosinophil functions in the treatment of atopic diseases, including bronchial asthma.

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humig or scyb9 or cxcl9
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L4          5141 FILE CAPLUS

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L78 ANSWER 37 OF 50 MEDLINE on STN DUPLICATE 24
ACCESSION NUMBER: 92159096 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 1741416
TITLE: Selective regulation of eosinophil degranulation by interleukin 1 beta.
AUTHOR: Baskar P; Pincus S H
CORPORATE SOURCE: Department of Dermatology, New England Medical Center Hospital, Boston, Massachusetts 02111.
CONTRACT NUMBER: AI123847 (NIAID)
AI16432 (NIAID)
SOURCE: Proceedings of the Society for Experimental Biology and Medicine. Society for Experimental Biology and Medicine (New York, N. Y.), (1992 Feb) 199 (2) 249-54.
Journal code: 7505892. ISSN: 0037-9727.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199203
ENTRY DATE: Entered STN: 19920410
Last Updated on STN: 19920410
Entered Medline: 19920324

AB Recent evidence confirms that cytokines such as IL-1, IL-4, IL-5, and GM-CSF may enhance or inhibit eosinophil function. Functions that are susceptible to modulation include eosinophil-mediated antibody-dependent damage of helminthic parasites, oxidative metabolism and degranulation. We have employed IgG and IgE-coated Sepharose beads to investigate selective modulation of IgG and IgE-mediated enzyme release by IL-1 beta. Both IgG and IgE-coated beads induced release of granular enzymes beta-glucuronidase and arylsulfatase. Enzyme release from IgG-stimulated eosinophils was inhibited by preincubation with IL-1 beta (100 pg/ml, P less than or equal to 0.05). In contrast, enzyme release by IgE-stimulated eosinophils was enhanced by IL-1 beta (100 pg/ml, P less than or equal to 0.05). These studies support the hypothesis that IL-1 beta has specific selective actions on eosinophil function. Furthermore, these actions on particle-stimulated enzyme release suggest that IgG and IgE mediated processes in eosinophils are differentially regulated.

L78 ANSWER 38 OF 50 MEDLINE on STN DUPLICATE 25
ACCESSION NUMBER: 92152455 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 1346737
TITLE: Use of cetirizine to investigate non-H1 effects of second-generation antihistamines.
AUTHOR: Townley R G; Okada C
CORPORATE SOURCE: Department of Medicine, Creighton University School of Medicine, Omaha, Nebraska.
SOURCE: Annals of allergy, (1992 Feb) 68 (2) 190-6. Ref: 20
Journal code: 0372346. ISSN: 0003-4738.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199203
ENTRY DATE: Entered STN: 19920405
Last Updated on STN: 19950206
Entered Medline: 19920316

AB In addition to their increased potency as H1 blockers and their nonsedating effects, the second-generation antihistamines have other unusual and potentially beneficial properties. Evidence is accumulating from several laboratories that at least one of these agents under investigation, cetirizine, may be effective in inhibiting the late reaction. The Johns Hopkins group showed that during the cutaneous late phase response (LPR), histamine release was not altered by cetirizine, 20 mg, pretreatment. The most dramatic effect of cetirizine was attenuation of inflammatory cell migration into the chamber. Eosinophils, neutrophils, and basophils were reduced by about 75% during hours 6 to 8. It can be concluded that cetirizine influences the LPR by causing a reduction in the inflammatory cell infiltrate. Cetirizine, 10 mg, orally once a day also induced a significant decrease in the wheal and flare skin reactions caused by pollen, histamine, and compound 48/80. Cetirizine inhibited eosinophil recruitment and platelet-activating factor (PAF) in skin chambers 24 hours after pollen challenge. We and others have studied the mechanisms of this effect. The release of eosinophil peroxidase induced by PAF and formyl- methionyleucyl/phenylalanine was not attenuated by cetirizine. At therapeutic concentrations, however, cetirizine has a potent inhibitory action in vitro on eosinophil chemotaxis induced either by formyl-methionyleucyl/phenylalanine or PAF and also on IgE-dependent stimulation of platelets. In a separate study in patients with chronic urticaria, cetirizine markedly reduced both the immediate wheal and flare induced by PAF and the delayed reaction at six hours. These results suggest that cetirizine acts on eosinophil migration to inhibit the late reaction.

L78 ANSWER 39 OF 50 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1990:417634 CAPLUS Full-text
DOCUMENT NUMBER: 113:17634
TITLE: Piroxicam affects collagen changes around experimental intestinal anastomoses
AUTHOR(S): Mastboom, Walter J. B.; Hendriks, T.; Van Elteren, P.; De Boer, H. H. M.
CORPORATE SOURCE: Dep. Gen. Surg., St. Radboud Univ. Hosp., Nijmegen, NL-6500 HB, Neth.
SOURCE: European Surgical Research (1990), Volume Date 1989, 21(6), 305-12
CODEN: EUSRBM; ISSN: 0014-312X
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The effects of piroxicam on postoperative changes of collagen, measured as hydroxyproline, concns. were measured around intestinal anastomoses in rats. Piroxicam, at a dose of 2 mg/kg/day, reduced the decrease of hydroxyproline concns. around colonic anastomoses during the first 3 days after the operation but also reduced the increase of hydroxyproline concns. observed at day 7 around ileal anastomoses in the control group. 10 Mg piroxicam/kg/day resulted in a 100% lethal peritonitis after the 5th postoperative day. It is suggested that piroxicam affects collagen metabolism by inhibiting granulocyte functions.

L78 ANSWER 40 OF 50 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1991:135714 CAPLUS Full-text
DOCUMENT NUMBER: 114:135714
TITLE: Latent inhibition of granulocyte function by cyclosporin A
AUTHOR(S): Kolb, Gerald; Eckle, Ilsebill; Bittner, Klaus; Mueller, Thomas; Havemann, Klaus; Lange, Harald
CORPORATE SOURCE: Dep. Intern. Med., Univ. Marburg, Marburg, D-3550, Germany

SOURCE: Immunobiology (1990), 181(1), 22-30
CODEN: IMMND4; ISSN: 0171-2985
DOCUMENT TYPE: Journal
LANGUAGE: English

AB This study set out to assess whether cyclosporin A (CsA) can change granulocyte function under therapy conditions or not. Thirty-seven patients, 3 mo-10 yr after kidney transplantation being under immunosuppressive treatment with CsA + prednisolone, azathioprine + prednisolone and under prednisolone alone underwent the study. Eighteen healthy persons served as a normal control group. Granulocyte function was tested ex vivo by chemiluminescence (CL) after stimulation with phorbolmyristate acetate (PMA) and with zymosan (Zym) activated autologous or pool-serum. The obtained data were correlated to corresponding serum or plasma levels of CsA, human leukocyte elastase (HLE) and neopterin. Comparing the 3 therapy groups with the healthy control and with each other no differences could be seen in median CL values; but there was a neg. correlation between CsA blood levels and maximum CL values of PMN. Such inhibition of CL could be calculated for Zym but not for PMA stimulated PMN; suggesting that the CsA mediated inhibition of granulocyte function may be only partial and restricted to phagocytosis. In addition, a pos. correlation between serum levels of human leukocyte elastase (HLE) and neopterin could be found. This indicates a simultaneous influence of CsA on both PMN and macrophages.

L78 ANSWER 41 OF 50 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1991:240166 CAPLUS Full-text
DOCUMENT NUMBER: 114:240166
TITLE: Anti-inflammatory action of zinc related to cutaneous pathology
AUTHOR(S): Dreno, B.; Boiteau, H. L.; Litoux, P.
CORPORATE SOURCE: Dep. Dermatol., Hotel Dieu, Nantes, 44035, Fr.
SOURCE: Met. Ions Biol. Med., Proc. Int. Symp., 1st (1990), 14-17. Editor(s): Collery, Philippe. Libbey: Paris, Fr.
CODEN: 56ZJAL
DOCUMENT TYPE: Conference
LANGUAGE: English

AB Erythrocyte and granulocyte Zn levels have different values between inflammatory and retentional acne. It is possible Zn act on inflammatory lesions by at least 2 mechanisms. By decreasing the Zn granulocyte level, Zn salts could inhibit granulocyte functions . An increase in Zn erythrocyte level could induce the activity of superoxide dismutase.

L78 ANSWER 42 OF 50 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1989:476337 CAPLUS Full-text
DOCUMENT NUMBER: 111:76337
TITLE: Effects of isoferritins on human granulocytes
AUTHOR(S): Hann, Hie Won L.; Stahlhut, Mark W.; Lee, Stephen; London, W. Thomas; Hann, Richard S.
CORPORATE SOURCE: Fox Chase Cancer Cent., Philadelphia, PA, USA
SOURCE: Cancer (New York, NY, United States) (1989), 63(12), 2492-6
CODEN: CANCAR; ISSN: 0008-543X
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Serum ferritin levels are often elevated in patients with certain cancers and these elevations are, in part, derived from the tumors. In such patients, the increased levels of serum ferritin are associated with a poor prognosis. The authors hypothesized that ferritins from tumor tissues may exert adverse

effects on human granulocytes that are involved in tumoricidal activity. Three granulocyte functions were tested: nitroblue tetrazolium test, phagocytosis, and production of hydrogen peroxide. The results supported the hypothesis: NBT reduction and phagocytosis are decreased in granulocytes exposed to ferritins, more so with tumor ferritins, than normal ferritin, and H2O2 production is less in granulocytes previously exposed to ferritins from tumor and nontumor tissues than cells not exposed to ferritins. However, the inhibitory effects of ferritins on H2O2 production can be reversed if granulocytes are further stimulated by phorbol myristate acetate (a membrane stimulant).

L78 ANSWER 43 OF 50 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN

ACCESSION NUMBER: 1990:76258 BIOSIS Full-text
DOCUMENT NUMBER: PREV199089044084; BA89:44084
TITLE: INHIBITION BY HALOTHANE BUT NOT BY ISOFLURANE OF OXIDATIVE RESPONSE TO OPSONIZED ZYMOSAN IN WHOLE BLOOD.
AUTHOR(S): LIENERS C [Reprint author]; REDL H; SCHLAG G; HAMMERSCHMIDT D E
CORPORATE SOURCE: HEMATOL DIV, DEP MED, BOX 480 UMHC, UNIV MINNESOTA, 500 SOUTHEAST HARVARD ST, MINNEAPOLIS, MINNESOTA 55455, USA
SOURCE: Inflammation, (1989) Vol. 13, No. 6, pp. 621-630. CODEN: INFLD4. ISSN: 0360-3997.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH
ENTRY DATE: Entered STN: 23 Jan 1990
Last Updated on STN: 24 Jan 1990

AB In an attempt to clarify some apparent discrepancies in reports of the effects of anesthetic agents upon granulocyte function, we studied the effects of halothane and isoflurane, using techniques that allowed us to perform the assays in whole blood and in sealed vials to prevent volatile gas evolution; assay gas concentrations were measured, rather than inferred. Chemiluminescence, superoxide production, and hydrogen peroxide production were assessed after presentation of opsonized zymosan as a phagocytic stimulus. Incubation with halothane led to a highly statistically significant dose-related inhibition of chemiluminescence (maximum 66%), H2O2 production (67%) and ·O2- production (61%), within the concentration range observed in blood from patients undergoing general anesthesia. In contrast, the presence of isoflurane led to no statistically significant changes in any of the functions measured. Cells harvested from patients undergoing elective halothane anesthesia showed the same functional inhibition, but for quantitative differences likely due to the inability to control for dilution effects in clinical samples. It has been suggested that halothane anesthesia may be associated with excess mortality in septic patients; although the results we report are readily reversible, their presence during a prolonged anesthesia could be harmful in a patient who is not immunologically normal and/or who is already infected. Careful clinical trials will be necessary to determine if isoflurane is a superior agent in this context.

L78 ANSWER 44 OF 50 MEDLINE on STN DUPLICATE 26

ACCESSION NUMBER: 90228401 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 2633928
TITLE: Piroxicam affects collagen changes around experimental intestinal anastomoses.
AUTHOR: Mastboom W J; Hendriks T; van Elteren P; de Boer H H
CORPORATE SOURCE: Department of General Surgery, St. Radboud University Hospital, Nijmegen, The Netherlands.

SOURCE: European surgical research. Europaische chirurgische Forschung. Recherches chirurgicales europeennes, (1989) 21 (6) 305-12.
Journal code: 0174752. ISSN: 0014-312X.
PUB. COUNTRY: Switzerland
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199005
ENTRY DATE: Entered STN: 19900706
Last Updated on STN: 19900706
Entered Medline: 19900525

AB The effects of piroxicam on postoperative changes of collagen--measured as hydroxyproline--concentrations were measured around intestinal anastomoses in rats. Piroxicam, in a dose of 2 mg/kg/day, significantly reduced the decrease of hydroxyproline concentrations around colonic anastomoses during the first 3 days after the operation but also reduced the increase of hydroxyproline concentrations observed at day 7 around ileal anastomoses in the control group. 10 mg piroxicam/kg/day resulted in a 100% lethal peritonitis after the 5th postoperative day. We suggest that piroxicam affects collagen metabolism by **inhibiting granulocyte functions.**

L78 ANSWER 45 OF 50 MEDLINE on STN
ACCESSION NUMBER: 89371417 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 2528270
TITLE: Eosinophils in bronchial asthma.
AUTHOR: Gorski P; Palczynski C
CORPORATE SOURCE: Department of Pneumonology and Allergology, Medical Academy of Lodz, Poland.
SOURCE: Allergologia et immunopathologia, (1989 Mar-Apr) 17 (2) 113-6. Ref: 40
Journal code: 0370073. ISSN: 0301-0546.
PUB. COUNTRY: Spain
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198910
ENTRY DATE: Entered STN: 19900309
Last Updated on STN: 19900309
Entered Medline: 19891003

AB A lot of recent works point out the role of the eosinophil as one of the most harmful cells in asthma. Eosinophilic granules contain strongly basiec cytotoxic proteins. Some of these proteins were shown to damage airway epithelial cells and degranulate basophils and mast cells. The concentration of eosinophil-derived major basic protein (MBP) in sputum is a good marker for clinical state in asthma. Extracellular MBP deposits were detected in lung tissue from patients who died of asthma. Several pieces of evidence indicate that eosinophil is stimulated to secrete its content in asthmatic reaction. Besides basic proteins the eosinophil can release other potent mediators of inflammation i.e. leukotriene C4 and PAF. Glucocorticosteroids, adrenergic agonists, disodium cromoglycate and specific immunotherapy were shown to **inhibit eosinophil function.**

L78 ANSWER 46 OF 50 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1988:148748 CAPLUS Full-text
DOCUMENT NUMBER: 108:148748

TITLE: Polynuclear iron complexes impair the function of polymorphonuclear granulocytes
AUTHOR(S): Hoepelman, I. M.; Jaarsma, E. Y.; Verhoef, J.; Marx, J. J. M.
CORPORATE SOURCE: Dep. Intern. Med., Univ. Hosp. Utrecht, Utrecht, 3500 CG, Neth.
SOURCE: British Journal of Haematology (1988), 68(3), 385-9
CODEN: BJHEAL; ISSN: 0007-1048
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The effects were studied of polynuclear and mononuclear Fe(III) on the polymorphonuclear leukocytes (PMN). Fe(III) in its polynuclear form (Fe:citrate 1:1) was deleterious for the phagocytic function of PMN, while the mononuclear form (Fe:citrate 1:20) was not toxic. Binding affinity of polynuclear Fe(III) for PMN was higher than of mononuclear Fe(III), and a considerable amount of bound Fe(III) was found in the cytosolic fraction of non-stimulated PMN. Limit dilution anal. of polynuclear complexes revealed that concns. as low as 25 μM Fe(III) impaired phagocytic function. The mol. weight of these complexes is similar to that of the non-transferrin plasma Fe found in the serum of patients with Fe overload. The toxic effects of small polynuclearl non-transferrin plasma Fe(III) complexes on PMN function may contribute to the development of infections in patients with Fe overload.

L78 ANSWER 47 OF 50 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1988:486466 CAPLUS Full-text
DOCUMENT NUMBER: 109:86466
TITLE: Inhibition of granulocyte function by steroids is not limited to corticoids. Studies with sex steroids
AUTHOR(S): Hammerschmidt, Dale E.; Knabe, Ann C.; Silberstein, Peter T.; Lamche, Herbert R.; Coppo, Patricia A.
CORPORATE SOURCE: Dep. Med., Univ. Hosp., Minneapolis, MN, 55455, USA
SOURCE: Inflammation (New York, NY, United States) (1988), 12(3), 277-84
CODEN: INFLD4; ISSN: 0360-3997
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A nonspecific physicochem. effect of steroids on the cell membrane was tested by determining the effects of 3 noncorticoid steroids on human granulocyte function. All 3 (conjugated equine estrogen, a synthetic progestogen, and a synthetic androgen) behaved in a manner analogous to corticoids at similar concns., inhibiting granulocyte aggregation, chemotaxis, and chemiluminescence, as well as binding to the granulocytes of the synthetic oligopeptide agonist formyl-Met-Leu-Phe. In addition estrogen reduced granulocyte membrane fluidity as assessed by ESR. The unique effects of extremely high-dose corticosteroids are thus not mediated via the glucocorticoid receptor, but result rather from physicochem. effects of the drugs on the membranes of effector cells.

L78 ANSWER 48 OF 50 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1985:178529 CAPLUS Full-text
DOCUMENT NUMBER: 102:178529
TITLE: Granulocyte recruitment and its inhibition
AUTHOR(S): Keller, H. U.
CORPORATE SOURCE: Inst. Pathol., Univ. Berne, Berne, Switz.
SOURCE: Handb. Inflammation (1985), Volume 5, 137-65.
Editor(s): Bonta, Ivan L.; Bray, Michael A.; Parnham, Michael J. Elsevier Biomed.: Amsterdam, Neth.
CODEN: 43WBAI

DOCUMENT TYPE: Conference; General Review
LANGUAGE: English
AB A review with 251 refs. of the different aspects of granulocyte recruitment that are related to cell migration (chemotaxis and inflammatory processes) and the effects of cytotaxins and drugs on such migration.

L78 ANSWER 49 OF 50 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1984:628394 CAPLUS Full-text
DOCUMENT NUMBER: 101:228394
TITLE: Effects of histamine agonists and antagonists on luminol-dependent chemiluminescence of granulocytes
AUTHOR(S): Ozaki, Yukio; Kume, Shoji; Ohashi, Tatsuya
CORPORATE SOURCE: Sch. Med., Univ. Tokyo, Tokyo, Japan
SOURCE: Agents and Actions (1984), 15(3-4), 182-8
CODEN: AGACBH; ISSN: 0065-4299
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Histamine inhibited luminol-dependent chemiluminescence (CL) of granulocytes in a concentration-dependent manner, with an ID50 of about 3 + 10-5 M. Dimaprit, a selective H2-agonist, produced a histamine-like effect. Furthermore, cimetidine, ranitidine, and TZU 0460, which are selective H2-antagonists, but not mepyramine, a selective H1-antagonist, blocked the inhibitory effect of histamine on CL. Thus, it may be concluded that the inhibitory effect of histamine is mediated via histamine H2-receptors. H1- and H2-antagonists per se, except at extremely high concns., had no effect on CL of granulocytes.

L78 ANSWER 50 OF 50 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
ACCESSION NUMBER: 1981:39834 BIOSIS Full-text
DOCUMENT NUMBER: PREV198120039834; BR20:39834
TITLE: A HIGH CHOLESTEROL DIET INHIBITS GRANULOCYTE FUNCTION IN RABBITS.
AUTHOR(S): LICHTENSTEIN I H [Reprint author]; MACGREGOR R R
CORPORATE SOURCE: UNIV PA SCH MED, PHILADELPHIA, PA, USA
SOURCE: Clinical Research, (1980) Vol. 28, No. 2, pp. 373A.
Meeting Info.: 37TH ANNUAL NATIONAL MEETING OF THE AMERICAN FEDERATION FOR CLINICAL RESEARCH, WASHINGTON, D.C., USA, MAY 10-12, 1980. CLIN RES.
CODEN: CLREAS. ISSN: 0009-9279.
DOCUMENT TYPE: Conference; (Meeting)
FILE SEGMENT: BR
LANGUAGE: ENGLISH

=> s rothenberg m?/au;s fulkerson p?/au
L84 280 FILE MEDLINE
L85 338 FILE BIOSIS
L86 227 FILE EMBASE
L87 244 FILE CAPLUS

TOTAL FOR ALL FILES
L88 1089 ROTHENBERG M?/AU

L89 40 FILE MEDLINE
L90 35 FILE BIOSIS
L91 27 FILE EMBASE

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L92          15 FILE CAPLUS

TOTAL FOR ALL FILES
L93         117 FULKERSON P?/AU

=> s l88 and l93
L94          10 FILE MEDLINE
L95          14 FILE BIOSIS
L96           9 FILE EMBASE
L97          11 FILE CAPLUS

TOTAL FOR ALL FILES
L98          44 L88 AND L93

=> dup rem l98
PROCESSING COMPLETED FOR L98
L99          17 DUP REM L98 (27 DUPLICATES REMOVED)

=> d 1-17 ibib abs

L99  ANSWER 1 OF 17      MEDLINE on STN
ACCESSION NUMBER:    2005562248      IN-PROCESS Full-text
DOCUMENT NUMBER:     PubMed ID: 16238782
TITLE:               Building a better mouse model: experimental models of
                     chronic asthma.
AUTHOR:              Fulkerson P C; Rothenberg M E; Hogan S
                     P
CONTRACT NUMBER:     P01 HL-076383-01 (NHLBI)
     R01 AI42242 (NIAID)
     R01 AI45898 (NIAID)
SOURCE:              Clinical and experimental allergy : journal of the British
                     Society for Allergy and Clinical Immunology, (2005 Oct) 35
                     (10) 1251-3.
                     Journal code: 8906443. ISSN: 0954-7894.
PUB. COUNTRY:        England: United Kingdom
DOCUMENT TYPE:       Editorial
LANGUAGE:            English
FILE SEGMENT:        NONMEDLINE; IN-PROCESS; NONINDEXED; Priority Journals
ENTRY DATE:          Entered STN: 20051022
                     Last Updated on STN: 20051111

L99  ANSWER 2 OF 17  CAPLUS  COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER:        2005:961475  CAPLUS Full-text
DOCUMENT NUMBER:         143:227950
TITLE:                   Cytokine inhibition of eosinophils
INVENTOR(S):             Rothenberg, Marc Elliot; Fulkerson,
                         Patricia Chandhok
PATENT ASSIGNEE(S):      USA
SOURCE:                  U.S. Pat. Appl. Publ., 33 pp., Cont.-in-part of U.S.
                         Ser. No. 752,659.
                         CODEN: USXXCO
DOCUMENT TYPE:           Patent
LANGUAGE:                English
FAMILY ACC. NUM. COUNT:  2
PATENT INFORMATION:

     PATENT NO.          KIND  DATE        APPLICATION NO.        DATE
     ---------------     ----  --------    --------------------   --------
     US 2005191273        A1   20050901    US 2005-91288          20050328
     US 2004141951        A1   20040722    US 2004-752659         20040107
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CA 2512090 AA 20040729 CA 2004-2512090 20040107
EP 1581166 A2 20051005 EP 2004-700562 20040107
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
PRIORITY APPLN. INFO.: US 2003-438412P P 20030107
US 2004-752659 A2 20040107
WO 2004-US199 W 20040107

AB The cytokine CXCL9 (MIG) inhibited eosinophil responses by a CCR3- and Rac2-dependent mechanism.

L99 ANSWER 3 OF 17 MEDLINE on STN DUPLICATE 1
ACCESSION NUMBER: 2005173175 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 15647285
TITLE: Identification of a cooperative mechanism involving interleukin-13 and eotaxin-2 in experimental allergic lung inflammation.
AUTHOR: Pope Samuel M; Fulkerson Patricia C; Blanchard Carine; Akei Hiroko Saito; Nikolaidis Nikolaos M; Zimmermann Nives; Molkentin Jeffery D; Rothenberg Marc E
CORPORATE SOURCE: Division of Allergy and Immunology, Cincinnati Children's Hospital Medical Center, University of Cincinnati College of Medicine, Cincinnati, Ohio 45229, USA.
CONTRACT NUMBER: R01 AI42242 (NIAID)
R01 AI45898 (NIAID)
R01 AI57803 (NIAID)
SOURCE: Journal of biological chemistry, (2005 Apr 8) 280 (14) 13952-61. Electronic Publication: 2005-01-12.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AY587128
ENTRY MONTH: 200506
ENTRY DATE: Entered STN: 20050405
Last Updated on STN: 20050622
Entered Medline: 20050621

AB Pulmonary eosinophilia, a hallmark pathologic feature of allergic lung disease, is regulated by interleukin-13 (IL-13) as well as the eotaxin chemokines, but the specific role of these cytokines and their cooperative interaction are only partially understood. First, we elucidated the essential role of IL-13 in the induction of the eotaxins by comparing IL-13 gene-targeted mice with wild type control mice by using an ovalbumin-induced model of allergic airway inflammation. Notably, ovalbumin-induced expressions of eotaxin-1 and eotaxin-2 mRNA in the lungs were almost completely dependent upon IL-13. Second, in order to address the specific role of eotaxin-2 in IL-13-induced pulmonary eosinophilia, we generated eotaxin-2 gene-deficient mice by homologous recombination. Notably, in contrast to observations made in eotaxin-1-deficient mice, eotaxin-2-deficient mice had normal base-line eosinophil levels in the hematopoietic tissues and gastrointestinal tract. However, following intratracheal IL-13 administration, eotaxin-2-deficient mice showed a profound reduction in airway eosinophilia compared with wild type mice. Most interestingly, the level of peribronchial lung tissue eosinophils in IL-13-treated eotaxin-2-deficient mice was indistinguishable from wild type mice. Furthermore, IL-13 lung transgenic mice genetically engineered to be deficient in eotaxin-2 had a marked reduction of luminal eosinophils. Mechanistic analysis identified IL13-induced eotaxin-2 expression by macrophages in a distinct lung compartment (luminal inflammatory

cells) compared with eotaxin-1, which was expressed solely in the tissue. Taken together, these results demonstrate a cooperative mechanism between IL-13 and eotaxin-2. In particular, IL-13 mediates allergen-induced eotaxin-2 expression, and eotaxin-2 mediates IL-13-induced airway eosinophilia.

L99 ANSWER 4 OF 17 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 2005341205 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 15802529
TITLE: CXCL9 inhibits eosinophil responses by a CCR3- and Rac2-dependent mechanism.
AUTHOR: **Fulkerson Patricia C**; Zhu Hongyan; Williams David A; Zimmermann Nives; **Rothenberg Marc E**
CORPORATE SOURCE: Department of Molecular Genetics, Biochemistry and Microbiology, University of Cincinnati College of Medicine, OH 45229-3039, USA.
CONTRACT NUMBER: P01 HL076383 (NHLBI)
R01 AI42242 (NIAID)
R01 AI45898 (NIAID)
SOURCE: Blood, (2005 Jul 15) 106 (2) 436-43. Electronic Publication: 2005-03-31.
Journal code: 7603509. ISSN: 0006-4971.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200508
ENTRY DATE: Entered STN: 20050706
Last Updated on STN: 20050819
Entered Medline: 20050818

AB Recently, inhibitory cytokine pathways for leukocyte chemoattraction and activation have been identified, but there is little insight into the operational mechanisms except for models that rely on simple receptor antagonism. We have previously identified the existence of a murine eosinophil inhibitory pathway mediated by the CXC chemokine ligand 9 (CXCL9, Mig [monokine induced by interferon-gamma]) that impressively blocks eosinophil chemoattraction and function, but the mechanism has remained elusive. We now demonstrate that Mig's inhibitory action extends beyond receptor antagonism alone. Notably, in addition to inhibiting eotaxin-induced filamentous actin (F-actin) formation and chemoattraction, Mig potently blocks platelet activating factor (PAF)- and leukotriene B4 (LTB4)-induced responses. Remarkably, Mig-treated eosinophils display an abnormal F-actin assembly in the absence of agonist stimulation. Additionally, Mig pretreatment inhibits eotaxin-induced activation of the Rho-guanosine triphosphatase (GTPase) Rac, and Rac2-deficient eosinophils demonstrate an impaired transmigration and actin polymerization response to eotaxin stimulation. Furthermore, Mig was unable to inhibit eotaxin-induced responses in Rac2-deficient eosinophils. Finally, using CCR3 gene-targeted cells, Mig's inhibitory activity is demonstrated to be mediated by CC chemokine receptor 3 (CCR3). Thus, by altering agonist-induced signaling and abrogating cytoskeletal reorganization by a Rac2-dependent mechanism, Mig markedly inhibits eosinophil responses to diverse stimuli. These results establish evidence that distinct chemokines can use CCR3 to induce opposing signals in eosinophils.

L99 ANSWER 5 OF 17 MEDLINE on STN DUPLICATE 3
ACCESSION NUMBER: 2005202035 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 15731505
TITLE: Expression and regulation of small proline-rich protein 2 in allergic inflammation.

AUTHOR: Zimmermann Nives; Doepker Matthew P; Witte David P; Stringer Keith F; **Fulkerson Patricia C**; Pope Samuel M; Brandt Eric B; Mishra Anil; King Nina E; Nikolaidis Nikolaos M; Wills-Karp Marsha; Finkelman Fred D; **Rothenberg Marc E**

CORPORATE SOURCE: Division of Allergy and Immunology, Cincinnati Children's Hospital Medical Center, 3333 Burnet Avenue, Cincinnati, OH 45229, USA.

CONTRACT NUMBER: R01 AI 42242 (NIAID)
R01 AI 45766 (NIAID)
R01 AI 45898 (NIAID)
R01 AI 5584 (NIAID)
R24 DK 06443 (NIDDK)

SOURCE: American journal of respiratory cell and molecular biology, (2005 May) 32 (5) 428-35. Electronic Publication: 2005-02-24.
Journal code: 8917225. ISSN: 1044-1549.

PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200506
ENTRY DATE: Entered STN: 20050420
Last Updated on STN: 20050701
Entered Medline: 20050630

AB Asthma is a complex inflammatory pulmonary disorder that is on the rise despite intense ongoing research. We aimed to elucidate novel pathways involved in the pathogenesis of asthma. Employing asthma models induced by different allergens (ovalbumin and Aspergillus fumigatus), we uncovered the involvement of two members of the small proline-rich protein (SPRR) family, SPRR2a and SPRR2b, known to be involved in epithelial differentiation but not allergic disease. In situ hybridization revealed induction of SPRR2 signal in a subset of bronchial epithelial cells and mononuclear cells associated with inflammation after allergen challenge. Allergen-induced SPRR2 mRNA accumulation in the lung occurred in a time-dependent manner, with peak expression 10-96 h after a second ovalbumin challenge. Transgenic overexpression of interleukin (IL)-13 in the lungs resulted in a marked increase of SPRR2 expression, and allergen-induced SPRR2 expression was significantly decreased in IL-13-deficient mice. Studies in gene-targeted mice revealed that allergen-induced SPRR2 was dependent upon STAT6. Finally, we aimed to determine if the induction of SPRR2 by allergen was tissue specific. Notably, SPRR2 was markedly increased in the small intestine after induction of allergic gastrointestinal inflammation. Thus, SPRR2 is an allergen- and IL-13-induced gene in experimental allergic responses that may be involved in disease pathophysiology.

L99 ANSWER 6 OF 17 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:589019 CAPLUS Full-text
DOCUMENT NUMBER: 141:122348
TITLE: Cytokine-containing composition and method to alter eosinophil function and recruitment
INVENTOR(S): **Rothenberg, Marc Elliot; Fulkerson, Patricia Chandhok**
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 24 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004141951	A1	20040722	US 2004-752659	20040107
CA 2512090	AA	20040729	CA 2004-2512090	20040107
WO 2004062585	A2	20040729	WO 2004-US199	20040107
WO 2004062585	A3	20041104		
W: AE, AE, AG, AL, AL, AM, AM, AM, AT, AT, AU, AU, AZ, AZ, BA, BB, BG, BG, BR, BR, BW, BY, BY, BZ, BZ, CA, CH, CN, CN, CO, CO, CR, CR, CU, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EC, EE, EE, EG, ES, ES, FI, FI, GB, GD, GE, GE, GH, GH, GH, GM, HR, HR, HU, HU, ID, IL, IN, IS, JP, JP, KE, KE, KG, KG, KP, KP, KP, KR, KR, KZ, KZ, KZ, LC, LK, LR, LS, LS, LT, LU, LV, MA, MD, MD, MG, MK, MN, MW, MX, MX, MZ				
EP 1581166	A2	20051005	EP 2004-700562	20040107
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
US 2005191273	A1	20050901	US 2005-91288	20050328
PRIORITY APPLN. INFO.:			US 2003-438412P	P 20030107
			US 2004-752659	A2 20040107
			WO 2004-US199	W 20040107

AB An allergen-induced chemokine with inhibitory activity on eosinophils, monokine induced by interferon γ (MIG) and/or an IFN-γ-inducible protein of 10 kDa (IP-10), is administered in a pharmaceutically acceptable dose and formulation. The composition is used for prophylaxis and therapy of diseases in which eosinophilia occurs and may be administered, for example, to patients with allergy and asthma.

L99 ANSWER 7 OF 17 MEDLINE on STN DUPLICATE 4
ACCESSION NUMBER: 2004627256 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 15585884
TITLE: Pulmonary chemokine expression is coordinately regulated by STAT1, STAT6, and IFN-gamma.
AUTHOR: **Fulkerson Patricia C**; Zimmermann Nives; Hassman Lynn M; Finkelman Fred D; **Rothenberg Marc E**
CORPORATE SOURCE: Department of Molecular Genetics, Biochemistry, and Microbiology, University of Cincinnati College of Medicine, Cincinnati, OH 45257, USA.
SOURCE: Journal of immunology (Baltimore, Md. : 1950), (2004 Dec 15) 173 (12) 7565-74.
Journal code: 2985117R. ISSN: 0022-1767.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200502
ENTRY DATE: Entered STN: 20041220
Last Updated on STN: 20050209
Entered Medline: 20050208

AB The expression of distinct chemokines within the asthmatic lung suggests that specific regulatory mechanisms may mediate various stages of asthmatic disease. Global transcript expression profiling was used to define the spectrum and kinetics of chemokine involvement in an experimental murine model of asthma. Seventeen chemokines were induced in the lungs of allergen-inoculated mice, as compared with saline-treated mice. Two (CXCL13 and CCL9) of the 17 identified chemokines have not previously been associated with allergic airway disease. Seven (7 of 17; CCL2, CCL7, CCL9, CCL11, CXCL1,

CXCL5, CXCL10) of the allergen-induced chemokines were induced early after allergen challenge and remained induced throughout the experimental period. Three chemokines (CXCL2, CCL3, and CCL17) were induced only during the early phase of the inflammatory response after the initial allergen challenge, while seven chemokines (CCL6, CCL8, CCL12, CCL22, CXCL9, CXCL12, and CXCL13) were increased only after a second allergen exposure. Unexpectedly, expression of only three chemokines, CCL11, CCL17, and CCL22, was STAT6 dependent, and many of the identified chemokines were overexpressed in STAT6-deficient mice, providing an explanation for the enhanced neutrophilic inflammation seen in these mice. Notably, IFN-gamma and STAT1 were shown to contribute to the induction of two STAT6-independent chemokines, CXCL9 and CXCL10. Taken together, these results show that only a select panel of chemokines (those targeting Th2 cells and eosinophils) is positively regulated by STAT6; instead, many of the allergen-induced chemokines are negatively regulated by STAT6. Collectively, we demonstrate that allergen-induced inflammation involves coordinate regulation by STAT1, STAT6, and IFN-gamma.

L99 ANSWER 8 OF 17 MEDLINE on STN DUPLICATE 5
ACCESSION NUMBER: 2004096460 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 14769916
TITLE: Negative regulation of eosinophil recruitment to the lung by the chemokine monokine induced by IFN-gamma (Mig, CXCL9).
AUTHOR: Fulkerson Patricia C; Zimmermann Nives; Brandt Eric B; Muntel Emily E; Doepker Matthew P; Kavanaugh Jessica L; Mishra Anil; Witte David P; Zhang Hongwei; Farber Joshua M; Yang Ming; Foster Paul S; Rothenberg Marc E
CORPORATE SOURCE: Department of Molecular Genetics, Biochemistry, and Microbiology, University of Cincinnati College of Medicine, 231 Bethesda Avenue, Cincinnati, OH 45257-0524, USA.
CONTRACT NUMBER: AI45898 (NIAID)
R01 AI42242 (NIAID)
SOURCE: Proceedings of the National Academy of Sciences of the United States of America, (2004 Feb 17) 101 (7) 1987-92. Electronic Publication: 2004-02-09. Journal code: 7505876. ISSN: 0027-8424.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200403
ENTRY DATE: Entered STN: 20040302
Last Updated on STN: 20040317
Entered Medline: 20040316

AB Experimental analysis of allergic airway inflammation (AAI) in animals and humans is associated with coordinate gene induction. Using DNA microarray analysis, we have identified a large panel of AAI signature genes. Unexpectedly, the allergen-challenged lung (a T helper 2 microenvironment) was found to be associated with the expression of T helper 1-associated CXCR3 ligands, monokine induced by IFN-gamma (Mig), and IFN-gamma-inducible protein of 10 kDa (IP-10). Here we report that Mig functions as a negative regulator of murine eosinophils. Whereas Mig was not able to induce chemotaxis of eosinophils, pretreatment with Mig induced a dose-dependent inhibition of chemoattractant-induced eosinophil transmigration in vitro. Moreover, i.v. administration of low doses of Mig (approximately 10-30 microg/kg) induced strong and specific dose-dependent inhibition of chemokine-, IL-13-, and allergen-induced eosinophil recruitment and, conversely, neutralization of Mig before allergen challenge increased airway eosinophilia. Importantly, Mig

also inhibited a CCR3-mediated functional response in eosinophils. These results indicate that the ultimate distribution and function of inflammatory cells within the allergic lung is dictated by a balance between positively and negatively regulatory chemokines. The identification of a naturally occurring eosinophil inhibitory chemokine pathway in vivo provides a strategic basis for future therapeutic consideration.

L99 ANSWER 9 OF 17 MEDLINE on STN DUPLICATE 6
ACCESSION NUMBER: 2004034924 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 14734765
TITLE: Transcript signatures in experimental asthma: identification of STAT6-dependent and -independent pathways.
AUTHOR: Zimmermann Nives; Mishra Anil; King Nina E; Fulkerson Patricia C; Doepker Matthew P; Nikolaidis Nikolaos M; Kindinger Laura E; Moulton Elizabeth A; Aronow Bruce J; Rothenberg Marc E
CORPORATE SOURCE: Division of Allergy and Immunology, Department of Pediatrics, Cincinnati Children's Hospital Medical Center, University of Cincinnati College of Medicine, Cincinnati, OH 45229, USA.
CONTRACT NUMBER: AI42242-05 (NIAID)
AI45898-04 (NIAID)
AI53479-01 (NIAID)
SOURCE: Journal of immunology (Baltimore, Md. : 1950), (2004 Feb 1) 172 (3) 1815-24.
Journal code: 2985117R. ISSN: 0022-1767.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200405
ENTRY DATE: Entered STN: 20040122
Last Updated on STN: 20040510
Entered Medline: 20040507

AB The analysis of polygenic diseases such as asthma poses a challenging problem. In an effort to provide unbiased insight into disease pathogenesis, we took an empirical approach involving transcript expression profiling of lung tissue from mice with experimental asthma. Asthmatic responses were found to involve sequential induction of 4.7% of the tested genome; notably, there was ectopic expression of a series of genes not previously implicated in allergic or pulmonary responses. Genes were widely distributed throughout all chromosomes, but preferentially included genes involved in immunity, development, and homeostasis. When asthma was induced by two independent experimental regimens, unique gene transcript profiles were found depending upon the mode of disease induction. However, the majority of genes were common to both models representing an asthma signature genome. Analysis of STAT6-deficient mice revealed that an unexpectedly large segment of the asthma genes were STAT6 independent; this correlated with sustained inflammatory events in these mice. Notably, induction of asthma in STAT6-deficient mice resulted in gene induction not seen in wild-type mice. These results raise concern that therapeutic blockade of STAT6 in the asthmatic setting may reprogram the genetic signature, resulting in alternative lung pathology, which we indeed observed in STAT6-deficient mice. These results provide unprecedented insight into the complex steps involved in the pathogenesis of allergic airway responses; as such, these results have significant therapeutic and clinical implications.

L99 ANSWER 10 OF 17 MEDLINE on STN DUPLICATE 7
ACCESSION NUMBER: 2004056222 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 14757645
TITLE: Foxa2 regulates alveolarization and goblet cell hyperplasia.
AUTHOR: Wan Huajing; Kaestner Klaus H; Ang Siew-Lan; Ikegami Machiko; Finkelman Fred D; Stahlman Mildred T; **Fulkerson Patricia C; Rothenberg Marc E**; Whitsett Jeffrey A
CORPORATE SOURCE: Division of Pulmonary Biology, Cincinnati Children's Hospital Medical Center, 3333 Burnet Avenue, Cincinnati, OH 45229-3039, USA.
CONTRACT NUMBER: HL56387 (NHLBI)
SOURCE: Development (Cambridge, England), (2004 Feb) 131 (4) 953-64.
Journal code: 8701744. ISSN: 0950-1991.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200403
ENTRY DATE: Entered STN: 20040204
Last Updated on STN: 20040327
Entered Medline: 20040326

AB The airways are lined by several distinct epithelial cells that play unique roles in pulmonary homeostasis; however, the mechanisms controlling their differentiation in health and disease are poorly understood. The winged helix transcription factor, FOXA2, is expressed in the foregut endoderm and in subsets of respiratory epithelial cells in the fetal and adult lung. Because targeted mutagenesis of the Foxa2 gene in mice is lethal before formation of the lung, its potential role in lung morphogenesis and homeostasis has not been determined. We selectively deleted Foxa2 in respiratory epithelial cells in the developing mouse lung. Airspace enlargement, goblet cell hyperplasia, increased mucin and neutrophilic infiltration were observed in lungs of the Foxa2-deleted mice. Experimental goblet cell hyperplasia caused by ovalbumin sensitization, interleukin 4 (IL4), IL13 and targeted deletion of the gene encoding surfactant protein C (SP-C), was associated with either absent or decreased expression of Foxa2 in airway epithelial cells. Analysis of lung tissue from patients with a variety of pulmonary diseases revealed a strong inverse correlation between FOXA2 and goblet cell hyperplasia. FOXA2 is required for alveolarization and regulates airway epithelial cell differentiation in the postnatal lung.

L99 ANSWER 11 OF 17 MEDLINE on STN DUPLICATE 8
ACCESSION NUMBER: 2004412954 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 15087305
TITLE: Expression and regulation of a disintegrin and metalloproteinase (ADAM) 8 in experimental asthma.
AUTHOR: King Nina E; Zimmermann Nives; Pope Samuel M; **Fulkerson Patricia C**; Nikolaidis Nikolaos M; Mishra Anil; Witte David P; **Rothenberg Marc E**
CORPORATE SOURCE: Division of Allergy and Immunology, Cincinnati Children's Hospital Medical Center, University of Cincinatti College of Medicine, Cincinnati, OH 45229, USA.
CONTRACT NUMBER: R01 AI42242 (NIAID)
R01 AI45898 (NIAID)
SOURCE: American journal of respiratory cell and molecular biology, (2004 Sep) 31 (3) 257-65. Electronic Publication: 2004-04-15.

Journal code: 8917225. ISSN: 1044-1549.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200410
ENTRY DATE: Entered STN: 20040820
Last Updated on STN: 20041006
Entered Medline: 20041005

AB Asthma, a complex chronic inflammatory pulmonary disorder, is on the rise despite intense ongoing research. To elucidate novel pathways involved in asthma pathogenesis, we used transcript expression profiling in a murine model of asthma. Employing asthma models induced by different allergens (ovalbumin and Aspergillus fumigatus) we uncovered the involvement of ADAM8, a member of a disintegrin and metalloproteinase (ADAM) family. In situ hybridization of mouse lungs revealed strong ADAM8 induction in peribronchial and perivascular inflammatory cells as well as in bronchiolar epithelial cells following allergen challenge. Sequence analysis of lung ADAM8 cDNA identified a novel splice variant of ADAM8 that contained an additional exon in juxtaposition to the transmembrane domain. Allergen-induced ADAM8 mRNA accumulation in the lung was dose- and time-dependent. Transgenic or pharmacologic delivery of interleukin (IL)-4 or IL-13 to the lungs resulted in a marked increase of ADAM8 expression. Gene-targeted mice studies revealed that ovalbumin-induced ADAM8 was largely dependent upon signal transducer and activator of transcription (STAT) 6 and the IL-4 receptor alpha-chain. Thus, ADAM8 is an allergen-, IL-4-, and IL-13-induced gene in the experimental asthmatic lung. Taken together with the role of ADAM33 in asthma, these results suggest that allergic lung responses involve the interplay of diverse members of the ADAM family.

L99 ANSWER 12 OF 17 MEDLINE on STN DUPLICATE 9
ACCESSION NUMBER: 2003532334 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 14610483
TITLE: Eotaxin-2 and IL-5 cooperate in the lung to regulate IL-13 production and airway eosinophilia and hyperreactivity.
AUTHOR: Yang Ming; Hogan Simon P; Mahalingam Surendran; Pope Sam M; Zimmermann Nives; **Fulkerson Patricia**; Dent Lindsay A; Young Ian G; Matthaei Klaus I; **Rothenberg Marc E**; Foster Paul S
CORPORATE SOURCE: Division of Molecular Biosciences, The John Curtin School of Medical Research, Australian National University, Canberra, ACT.
CONTRACT NUMBER: R01 AI42242-02 (NIAID)
R01 AI45898-01 (NIAID)
SOURCE: Journal of allergy and clinical immunology, (2003 Nov) 112 (5) 935-43.
Journal code: 1275002. ISSN: 0091-6749.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200312
ENTRY DATE: Entered STN: 20031113
Last Updated on STN: 20031220
Entered Medline: 20031219

AB BACKGROUND: Eotaxin-2 is a member of the eotaxin subfamily of CC chemokines that display eosinophil-specific, chemotactic properties and has been associated with allergic disorders. However, the contribution of eotaxin-2 to the development of defined pathogenic features of allergic disease remains to

be defined. OBJECTIVE: We sought to determine whether eotaxin-2 was a cofactor with IL-5 for the regulation of pulmonary eosinophilia and to identify the combined role of these molecules in the induction of phenotypic characteristics of allergic lung disease. METHODS: We instilled recombinant eotaxin-2 into the airways of wild-type mice that had been treated systemically with IL-5 or into IL-5-transgenic mice and characterized pulmonary eosinophil numbers, IL-13 production, and airway hyperreactivity (AHR) to methacholine. Mice deficient in the IL-4 receptor alpha-chain, IL-13, and signal transducers and activators of transcription 6 or mice treated with anti-CCR3 monoclonal antibody were also used. RESULTS: Eotaxin-2 and IL-5 cooperatively promoted eosinophil accumulation, IL-13 production, and AHR to methacholine. Neither eotaxin-2 nor IL-5 alone induced these features of allergic disease. IL-13 production was critically dependent on eotaxin-2- and IL-5-regulated eosinophilia, which predisposed to the development of AHR. AHR was dependent on IL-13 and signaling through the IL-4R alpha-chain and signal transducers and activators of transcription 6 pathways and the presence of eosinophils in the lung. CONCLUSION: These investigations demonstrate important cooperativity between eotaxin-2, IL-5, and IL-13 signaling systems and eosinophils for the development of hallmark features of allergic disease of the lung.

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ACCESSION NUMBER: 2003:239414 BIOSIS Full-text
DOCUMENT NUMBER: PREV200300239414
TITLE: Induction of resistin-like molecule beta (RELM-beta) by respiratory allergen, IL-4, IL-13, and STAT6 in experimental asthma.
AUTHOR(S): DeBrosse, C. W. [Reprint Author]; Zimmermann, N. [Reprint Author]; King, N. E. [Reprint Author]; Pope, S. M. [Reprint Author]; **Fulkerson, P. C.** [Reprint Author]; Mishra, A. [Reprint Author]; **Rothenberg, M. E.** [Reprint Author]
CORPORATE SOURCE: Division of Allergy and Immunology, Cincinnati Children's Hospital Medical Center, Cincinnati, OH, USA
SOURCE: Journal of Allergy and Clinical Immunology, (April 2003) Vol. 111, No. 4, pp. 906. print.
Meeting Info.: 60th Anniversary Meeting of the American Academy of Allergy, Asthma and Immunology (AAAAI). Denver, CO, USA. March 07-12, 2003. American Academy of Allergy, Asthma and Immunology.
CODEN: JACIBY. ISSN: 0091-6749.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 21 May 2003
Last Updated on STN: 21 May 2003

L99 ANSWER 14 OF 17 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN

ACCESSION NUMBER: 2003:360054 BIOSIS Full-text
DOCUMENT NUMBER: PREV200300360054
TITLE: Eotaxin-2 is critical for eosinophil recruitment into the airway lumen in experimental asthma.
AUTHOR(S): Pope, S. M. [Reprint Author]; Zimmermann, N. [Reprint Author]; **Fulkerson, P. C.** [Reprint Author]; **Rothenberg, M. E.** [Reprint Author]
CORPORATE SOURCE: Allergy and Immunology, Children's Hospital of Cincinnati, Cincinnati, OH, USA

SOURCE: Journal of Allergy and Clinical Immunology, (February 2003) Vol. 111, No. 2 Abstract Supplement, pp. S340. print. Meeting Info.: AAAAI 60th Anniversary Meeting. Denver, CO, USA. March 07-12, 2003. American Academy of Allergy, Asthma and Immunology. CODEN: JACIBY. ISSN: 0091-6749.
DOCUMENT TYPE: Conference; (Meeting) Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 6 Aug 2003 Last Updated on STN: 6 Aug 2003

L99 ANSWER 15 OF 17 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
ACCESSION NUMBER: 2003:359850 BIOSIS Full-text
DOCUMENT NUMBER: PREV200300359850
TITLE: The chemokine monokine induced by IFN-g (Mig, CXCL9) is a potent inhibitor of eosinophils in vitro and in vivo.
AUTHOR(S): **Fulkerson, P. C.** [Reprint Author]; Zimmermann, N.; Brandt, E. B.; Muntel, E. E.; Kavanaugh, J.; Mishra, A.; Ming, Y.; Foster, P. S.; Farber, J. M.; **Rothenberg, M. E.**
CORPORATE SOURCE: Department of Molecular Genetics, Biochemistry and Microbiology, College of Medicine, University of Cincinnati, Cincinnati, OH, USA
SOURCE: Journal of Allergy and Clinical Immunology, (February 2003) Vol. 111, No. 2 Abstract Supplement, pp. S290. print. Meeting Info.: AAAAI 60th Anniversary Meeting. Denver, CO, USA. March 07-12, 2003. American Academy of Allergy, Asthma and Immunology. CODEN: JACIBY. ISSN: 0091-6749.
DOCUMENT TYPE: Conference; (Meeting) Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 6 Aug 2003 Last Updated on STN: 6 Aug 2003

L99 ANSWER 16 OF 17 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
ACCESSION NUMBER: 2003:347623 BIOSIS Full-text
DOCUMENT NUMBER: PREV200300347623
TITLE: Induction of resistin-like molecule beta (RELM-beta) by respiratory allergen, IL-4, IL-13, and STAT6 in experimental asthma.
AUTHOR(S): DeBrosse, C. W. [Reprint Author]; Zimmermann, N. [Reprint Author]; King, N. E. [Reprint Author]; Pope, S. M. [Reprint Author]; **Fulkerson, P. C.** [Reprint Author]; Mishra, A. [Reprint Author]; **Rothenberg, M. E.** [Reprint Author]
CORPORATE SOURCE: Division of Allergy and Immunology, Cincinnati Children's Hospital Medical Center, Cincinnati, OH, USA
SOURCE: Journal of Allergy and Clinical Immunology, (February 2003) Vol. 111, No. 2 Abstract Supplement, pp. S187. print. Meeting Info.: AAAAI 60th Anniversary Meeting. Denver, CO, USA. March 07-12, 2003. American Academy of Allergy, Asthma and Immunology. CODEN: JACIBY. ISSN: 0091-6749.
DOCUMENT TYPE: Conference; (Meeting) Conference; Abstract; (Meeting Abstract)
LANGUAGE: English

ENTRY DATE: Entered STN: 30 Jul 2003
Last Updated on STN: 30 Jul 2003

L99 ANSWER 17 OF 17 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
ACCESSION NUMBER: 2002:289930 BIOSIS Full-text
DOCUMENT NUMBER: PREV200200289930
TITLE: Genomic analysis of chemokine and chemokine receptor expression in experimental allergic asthma.
AUTHOR(S): **Fulkerson, Patricia C.** [Reprint author]; Zimmermann, Nives [Reprint author]; Moulton, Elizabeth A. [Reprint author]; Aronow, Bruce J. [Reprint author]; **Rothenberg, M. E.** [Reprint author]
CORPORATE SOURCE: Children's Hospital of Cincinnati, Cincinnati, OH, USA
SOURCE: Journal of Allergy and Clinical Immunology, (January, 2002) Vol. 109, No. 1 Supplement, pp. S175. print.
Meeting Info.: 58th Annual Meeting of the American Academy of Allergy, Asthma and Immunology. New York, NY, USA. March 01-06, 2002. American Academy of Allergy Asthma and Immunology.
CODEN: JACIBY. ISSN: 0091-6749.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 15 May 2002
Last Updated on STN: 15 May 2002

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(FILE 'REGISTRY' ENTERED AT 10:12:55 ON 14 DEC 2005)
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FILE 'MEDLINE, BIOSIS, EMBASE, CAPLUS' ENTERED AT 10:15:56 ON 14 DEC 2005
L1 2864 FILE MEDLINE
L2 3052 FILE BIOSIS
L3 3080 FILE EMBASE
L4 5141 FILE CAPLUS
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L5 14137 S MIG OR MONOKINE INDUCE? (L) (IFN OR INTERFERON)(W)GAMMA OR CH

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FILE 'MEDLINE, BIOSIS, EMBASE, CAPLUS' ENTERED AT 10:17:08 ON 14 DEC 2005
L6 1395 FILE MEDLINE
L7 1930 FILE BIOSIS
L8 1336 FILE EMBASE
L9 1909 FILE CAPLUS
TOTAL FOR ALL FILES
L10 6570 S RECEPTOR INTERNAL?
L11 101536 FILE MEDLINE
L12 76683 FILE BIOSIS
L13 88372 FILE EMBASE
L14 34724 FILE CAPLUS
TOTAL FOR ALL FILES
L15 301315 S ASTHMA OR BRONCHIAL DISEASE OR BRONCHODILATOR?
L16 1119 FILE MEDLINE
L17 770 FILE BIOSIS
L18 860 FILE EMBASE

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L19          761 FILE CAPLUS
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L21        33257 FILE MEDLINE
L22         8393 FILE BIOSIS
L23        10344 FILE EMBASE
L24        11476 FILE CAPLUS
     TOTAL FOR ALL FILES
L25        63470 S ERK 1 OR ERK1 OR CEK1 PROTEIN (L)CANDIDA ALBICAN? OR FUNGAL P
L26        12376 FILE MEDLINE
L27        11541 FILE BIOSIS
L28        11544 FILE EMBASE
L29         9145 FILE CAPLUS
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L30        44606 S (EOSINOPHIL OR GRANULOCYTE?)(L)(RECRUIT? OR FUNCTION?)
L31            4 FILE MEDLINE
L32            3 FILE BIOSIS
L33            4 FILE EMBASE
L34            4 FILE CAPLUS
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L36            4 DUP REM L35 (11 DUPLICATES REMOVED)
L37           29 FILE MEDLINE
L38           30 FILE BIOSIS
L39           44 FILE EMBASE
L40           67 FILE CAPLUS
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L41          170 S L5 AND L15
L42           29 FILE MEDLINE
L43           30 FILE BIOSIS
L44           44 FILE EMBASE
L45           65 FILE CAPLUS
     TOTAL FOR ALL FILES
L46          168 S L5 AND ASTHMA
L47           29 FILE MEDLINE
L48           30 FILE BIOSIS
L49           44 FILE EMBASE
L50           67 FILE CAPLUS
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L51          170 S L41 OR L46
L52           18 FILE BIOSIS
L53           20 FILE EMBASE
L54           36 FILE CAPLUS
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L55           74 S L51
L56           48 DUP REM L55 (26 DUPLICATES REMOVED)
L57            7 FILE MEDLINE
L58            3 FILE BIOSIS
L59            1 FILE EMBASE
L60            9 FILE CAPLUS
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L61           20 S L20 AND L25
L62           12 DUP REM L61 (8 DUPLICATES REMOVED)
L63         3259 FILE MEDLINE
L64         2898 FILE BIOSIS
L65         3029 FILE EMBASE
L66         3041 FILE CAPLUS
     TOTAL FOR ALL FILES
L67        12227 S INHIBIT? AND L30
L68          101 FILE MEDLINE
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L69          101 FILE BIOSIS
L70           97 FILE EMBASE
L71          115 FILE CAPLUS
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L72          414 S (EOSINOPHIL OR GRANULOCYTE)(A)(FUNCTION OR RECRUIT?)(5A)INHIB
L73           28 FILE MEDLINE
L74           23 FILE BIOSIS
L75           25 FILE EMBASE
L76           40 FILE CAPLUS
     TOTAL FOR ALL FILES
L77          116 S (EOSINOPHIL OR GRANULOCYTE)(A)(FUNCTION OR RECRUIT?)(A)INHIBI
L78           50 DUP REM L77 (66 DUPLICATES REMOVED)
L79            0 FILE MEDLINE
L80            0 FILE BIOSIS
L81            0 FILE EMBASE
L82            0 FILE CAPLUS
     TOTAL FOR ALL FILES
L83            0 S L77 AND L5
L84          280 FILE MEDLINE
L85          338 FILE BIOSIS
L86          227 FILE EMBASE
L87          244 FILE CAPLUS
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L88         1089 S ROTHENBERG M?/AU
L89           40 FILE MEDLINE
L90           35 FILE BIOSIS
L91           27 FILE EMBASE
L92           15 FILE CAPLUS
     TOTAL FOR ALL FILES
L93          117 S FULKERSON P?/AU
L94           10 FILE MEDLINE
L95           14 FILE BIOSIS
L96            9 FILE EMBASE
L97           11 FILE CAPLUS
     TOTAL FOR ALL FILES
L98           44 S L88 AND L93
L99           17 DUP REM L98 (27 DUPLICATES REMOVED)

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